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ORIGINAL ARTICLE

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Periprocedural Analgesia and Sedation in Air Enema Reduction for Intussusception.
A Retrospective Australian Cohort Study

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All authors contributed to the concept of this paper, drafting and revising the manuscript; and agree to be accountable for the accuracy and integrity of the work.

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Key words

Child; Humans; Analgesia; Intussusception; Enema; Pain management;

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ABSTRACT

Aim:

Periprocedural analgesia or sedation for air enema reduction (AER) of intussusception is a matter of debate. We set out to review Australian periprocedural pain management in AER.

Methods:

Retrospective electronic medical record review of emergency department presentations of intussusception at an Australian children's hospital over two years for periprocedural analgesia and sedation and short-term outcomes.

Results:

73 patients (mean age 23 months) had ultrasound (US) confirmed intussusception. Prior to AER, analgesia was administered to 61/73 (83.5%) patients. Opioids were administered in 48/73 (65.8%) - and 8/73 (11.0 %) received sedation. 13/73 (17.8%, 95% CI 9.0-26.6) had spontaneously reduced; 60/73 that underwent primary AER had successful reduction in 54 (90.0%, 95% CI 82.4-97.6). A total of 7 patients required surgery. No AER attempts were complicated by bowel perforation.

Conclusions:

The use of periprocedural analgesia for AER in this Australian series was common, whilst sedation use was infrequent. No perforations occurred.

Key words

Child; Humans; Analgesia; Intussusception; Enema; Pain management;

What is already known on this topic

1. Periprocedural analgesia or sedation for air enema reduction (AER) of intussusception is a matter of debate, with opponents citing concerns about an associated increased risk of bowel perforation.
2. Australian practice regarding periprocedural pain management for AER of intussusception is unknown.

What this paper adds

1. In a 2-year cohort study of 73 planned AERs at a tertiary children's hospital the use of periprocedural analgesia for AER was common but sedation use was infrequent.
2. No bowel perforations associated with AER occurred in this series.
3. There is scope for improved periprocedural care in terms of pain management and a reduction in variation of care for AER.

INTRODUCTION

Intussusception is one of the most common causes of paediatric abdominal emergency presentations. It typically affects children between six months and two years of age.^{1,2} Intussusception most often follows a viral or bacterial trigger, with pathological lead points accounting for less than five percent of cases.³⁻⁵ The clinical diagnosis is confirmed with abdominal ultrasound imaging, which demonstrates both the presence of an intussusception (e.g. 'target' sign) as well as the extent and state of bowel involved. Once the diagnosis is confirmed, early retrograde enema under radiologic guidance is favoured, a commonly used example being air enema reduction (AER) under fluoroscopic guidance.⁶ Operative management is limited to that minority of cases who present with established signs of complications (e.g. peritonism, bowel perforation), or for whom AER is complicated by either unsuccessful reduction or perforation.²

AER is invasive and may be unpleasant for the child and family and can be challenging for the treating team. Whilst one study reported that over 90% of children with intussusception presented to the ED with pain⁷, it is unknown how much additional pain can be attributed to the AER procedure *per se*. A child presenting with intussusception may have a reduced conscious state due to the associated third-space losses and hypovolaemia. This and fluid resuscitation notwithstanding, the resistive, uncooperative child may require a prolonged AER procedure and additional attempts to successfully reduce the intussusception. Thus, this has been suggested to increase the procedural risks of perforation and radiation exposure.⁸ Whilst no studies have evaluated discomfort and pain severity during AER for intussusception, children undergoing colonoscopy are perceived to experience high levels of discomfort and benefit from procedural sedation and analgesia with routine provision of deep sedation.⁹ The traditional views in the literature for AER of intussusception is that analgesia and sedation may increase the risk of perforation, mask the signs of shock and decrease the success of reduction.¹⁰

The evidence regarding pre-procedural analgesia and sedation for the management of intussusception is limited and has led to a range of pre-procedural management guidelines.¹¹⁻¹³ Past studies have shown no significant difference in AER success with and without sedation. A pig model showed that the loss of straining (Valsalva manoeuvre) under deep sedation resulted in higher colonic perforation rates from enema reduction.^{14, 15} This has traditionally swayed recommendations away from using sedative agents as premedication for AER.⁵ More recent human literature provide contrary evidence

showing that general anaesthesia and procedural sedation increases successful reduction rates, decreases procedure duration, recurrence rates and may facilitate earlier discharge.^{8,16} The Royal Children's Hospital (RCH), Melbourne, Australia, clinical practice guidelines for intussusception suggests the administration of analgesia as part of management, but not qualify this suggestion with reference to premedication for AER in particular or make recommendations regarding indication or agents for sedation for AER.¹¹ In contrast, the clinical practice guidelines from Great Ormond St Hospital, a large British quaternary paediatric centre, specifies that analgesia and sedation not be used due to concerns it may increase the risk of complications.¹²

There are no Australian data on the use of pre-procedural analgesia and/or procedural sedation for AER. This study's aim was to assess current use of periprocedural analgesia and sedation use and document success and complications of AER at a large Australian children's hospital.

METHOD

Design and Setting

This single centre retrospective cohort study of clinical practice for AER was conducted at RCH, Melbourne, the largest tertiary paediatric centre in Australia. The RCH Emergency Department (RCH ED) has an annual census of 90,000 children. The study was approved by the local Human Research Ethics committee (HREC 38155A).

Patients were identified via a search of radiologically confirmed intussusceptions following the introduction of the hospital-wide integrated electronic medical record system (EMR; Epic, Wisconsin, USA) between May 2016 until June 2018.

Inclusion criteria

- Children aged less than 18 years presenting to the RCH ED AND
- ICD diagnosis of intussusception (ICD 10 code K56.1) confirmed on imaging AND
- Prescribed AER as first line management

Exclusion criteria

- Suspected cases of intussusception later disproven via an alternative diagnosis OR
- Cases of intussusception not prescribed AER

Study procedure

All children presenting to the RCH ED over the 25-month study period with a confirmed diagnosis of intussusception AND prescribed AER were identified through an EMR search using the ICD code

applied at discharge from the ED. In order to ensure that all cases had been identified, we also used a separate search algorithm for patients prescribed AER in EMR; charts of all such identified cases were also reviewed.

Outcomes

Primary outcome was the use of analgesia or sedation prior to undergoing AER and proportion of successful reductions.

Secondary outcome measures included:

- Short term outcomes (failed reduction, operative management, intussusception recurrence within 48 hours of AER (early recurrence))
- Complications during or following reduction including no clinical, radiological or operative bowel perforation at any time after the AER.

Definitions

- Intussusception was defined as RCH radiologist reported intussusception on ultrasound.
- Medication doses were counted as periprocedural if they had been administered within 4 hours (simple analgesia), 2 hours (opioids) or 1 h (sedative agents) prior to or during AER.
- Successful reduction was defined as the presence of reflux air into the distal ileum with disappearance of the invaginated soft tissue mass as reported by a radiology physician at RCH.
- Sedation was defined as use of a sedative or anaesthetic agent with the intention of inducing a state of sedation, not anaesthesia.
- Sedation related adverse events as recorded in EMR by medical or nursing staff; reported adverse events were coded using the definitions provided by Bhatt et al.¹⁷

Database and Analysis

A Research Electronic Data Capture (REDCap)¹⁸ database was created and the following variables were collected:

- Demographics
- Prior history of intussusception and underlying conditions
- Symptoms on ED presentation
- Investigations
- Time from ED presentation to diagnosis, reduction, admission and discharge
- Medications and other treatments administered prior to reduction
- Medication side effects/ adverse outcomes prior to operation (if required) or patient discharge

- Reduction methods and attempts
- Complications during reduction
- Staff involved
- Operative reduction
- Likely lead point
- Rates of early recurrence (48 hours post reduction)

No sedations scores were used or recorded.

Data was analysed using Stata (StataCorp. Stata Statistical Software: Release 15. TX: StataCorp LLC: College Station, USA; 2017). We undertook descriptive analysis of the data with 95% confidence intervals (CI) for key percentages.

RESULTS

During the 25-month study period, a total of 73 patients were identified who satisfied the inclusion and exclusion criteria for this study; 41/73 (56.2%) were male with a mean age of patients was 23 months (range 2-103 months). Of these 73 patients, 66/73 were identified according to ICD-10 diagnosis of intussusception, together with imaging confirmation of intussusception and first line treatment with AER. A further seven cases were identified following search for patients for whom an AER was ordered in the hospital EMR, to make up total of 73 study patients. Interestingly, ICD-10 coding identified another 56 patients, who were subsequently excluded as they transpired not have intussusception after detailed exploration of their medical record. The vast majority of these 56 patients had abdominal pain of unknown aetiology or irritability, but no ultrasound findings of intussusception.

The most common presenting signs and symptoms (**Table 1**) were abdominal pain with or without drawing up of legs, irritability and vomiting. The average duration of symptoms leading up to presentation for medical care was 1.8 days. Abdominal ultrasound confirmed the diagnosis in all patients. Pathological lead points were identified in 5/73 (6.8%) cases; two duplication cysts (identified at surgery); one appendix (identified on ultrasound); one classified as either a Meckel's diverticulum or duplication cyst.

Analgesia was administered to 61/73 (83.5%) intussusception patients. Simple analgesia with paracetamol or ibuprofen was given to 28/73 (38.4%) patients within 4 h prior to AER (**Table 2**).

Opioid analgesia within 2 h was administered in most patients as part of ED management or as premedication in preparation for AER (48/73; 65.8% 95% CI 75.0-92.1); intravenous (IV) morphine (n = 41; 56.1%), intranasal (IN) (n = 9; 12.3%); IV fentanyl (n=8; 11.0%); oral oxycodone (n=2; 2.7%). IV morphine was administered an average of 37.5 minutes before AER; IN fentanyl 27 minutes before AER; IV fentanyl 53 minutes before AER and oral oxycodone 67 minutes before AER.

Sedative agents were administered as premedication prior to or during the procedure in 8/73 (11.0% 95% CI 4-18.6), mainly midazolam. A small number of patients received propofol (2), ketamine (1) or nitrous oxide (1). The total average time between administration of sedative and undergoing AER was 17 minutes. Midazolam was administered an average of 17 minutes before AER; Propofol 8 minutes before AER; Ketamine 26 minutes; Nitrous was commenced 20 minutes before AER and continued throughout the procedure. Of the 8 patients who had received sedative agents, 8 had also received opioid analgesia. There were no recorded analgesia- or sedation- related adverse events.

Out of the total cohort of 73 patients, 60/73 (82.1%, 95% CI 73.3-90.1) patients underwent AER. The remaining 13/73 (17.8%, 95% CI, 9.0-26.6) did not undergo AER on the basis of a pre-enema ultrasound demonstrating spontaneous resolution of intussusception. None of the non-AER group had further complications or recurrence of intussusception. Eight of these non-AER 13 patients received opioid analgesia as part of their initial intussusception management in ED, but none received sedation.

Of the 60 patients who underwent AER, 54/60 (90.0 %, 95% CI 82.4-97.6) had successful primary reduction with AER and 6/60 (10.0 %, 95% 2.4-17.6) failed primary AER (**Table 3**). Five of 60 (8.3%) had two attempts, 5/60 (8.3%) three attempts and 5/60 (8.3%) more than three attempts. Of those patients experiencing only a single AER attempt, 37/47 (78.7%) received opioid analgesia, as compared with patients with multiple AER attempts who all received opioid analgesia. Periprocedural sedation was used in 6 patients that underwent a single AER attempt and 2 patients that had multiple AER attempts.

Forty eight of 60 (80.0%, 95% CI 69.9-90.1) patients had successful primary AER with no recurrence whilst six patients (10%, 95% CI 2.4-7.6) who had successful primary AER had recurrence within 48 hours. All six had periprocedural opioid analgesia and none had sedation. Five from this group

achieved successful resolution with repeat secondary AER, with the remaining patient failing secondary AER and eventually proceeding to laparotomy as described below.

Of the cohort of 73 included patients, seven (11.7 %, 95% 3.6-19.8) underwent surgery as part of their intussusception management. Failure of primary AER was the indication for surgery in six patients. Five patients failed primary AER despite three or more attempts at AER. All five received IV morphine as analgesia, with one also receiving ketamine and another receiving midazolam with nitrous oxide in addition to their opioid analgesia. Four of these five patients underwent bowel resections, and no cases required stoma formation. A sixth patient failed primary AER, albeit the decision for surgery was made after only a single unsuccessful AER attempt. The decision to abandon AER in this case was due to a suspected ileo-ileal intussusception, which is not amenable to AER, and this pathology was confirmed at surgery. The seventh operative patient underwent successful primary AER on the first attempt, but had recurrence of the intussusception within 48 hours with failure of the repeat AER attempt. This patient required surgical reduction, but did not require resection.

Overall in the total cohort, there were no perforations (0%, 95% CI 0.0- 0.2). This perforation rate includes both radiologic and intraoperative findings, as well as equating uncomplicated admission and short-term clinical follow up with absence of perforation. All patients that underwent surgery recovered without complications post operatively. The mean length of stay for all cases was 1.5 days (range 0.9-9.7 days), with an expectedly longer average length of stay for operative cases (1.64 days, range 3.2-9.7 days). There were no reported deaths.

DISCUSSION

This is the first Australian study to explore specifically the role of periprocedural analgesia for AER in intussusception. The key findings were that in this tertiary children's hospital the use of periprocedural analgesia for AER management of intussusception was common, but sedation use was infrequent. The favoured approach was opioid analgesia, being administered to two thirds of our AER cohort, principally as IV morphine. The frequency of these prescriptions suggests that there is clinician awareness of the pain associated with intussusception and AER. Similar to other studies evaluating presenting symptoms of intussusception, pain at presentation was also the predominant described symptom in our cohort of patients.⁷

Alongside the clinical presentation, the management decision-making represented in this study is likely also influenced by the local RCH CPG, which states “give analgesia (usually morphine)”. Whilst this and other CPGs do not mandate actions, so as to over-rule clinician acumen, the local preference for opioid analgesia is likely both reflected and reinforced by these guidelines. Be this as it may, our study reflects both clinician and institutional ‘comfort’ with periprocedural analgesia for AER in intussusception, undeterred by the more historical and porcine model-based concerns that such analgesia may be at the cost of an increased risk of bowel perforation.¹⁴ In this study spanning a more than two year period, we did not see cases of bowel perforation or sepsis related to AER associated with our prevalent use of opioid analgesia. These results are different to a recent retrospective study of 214 children undergoing AER for intussusception who reported three bowel perforations all of which were below the age of 5 months and had received propofol based sedation.¹⁰

The number of cases of intussusception (73) identified over the study period translate into 4.3 patients/10,000 ED presentations. The success rate of primary AER evident in our study (90%) is consistent with rates of 89% to 92% reported in other recent reports that investigated AERs in intussusception using sedation and analgesia in tertiary paediatric specialist centres.^{6, 10, 16} A meta-analysis review of intussusception enema reduction, shows an early recurrence rate of 2.7-6.6% in the first 48 hours, irrespective of enema type.¹⁹ In our series, we observed an early recurrence rate (within 48 hours) of 10%, albeit this is unlikely to represent a statistically significant difference from these other reported rates.

Our review of the literature indicates that there are no prospective observational studies to assess the pain experience of children undergoing AER and the safety of sedation in AER. Both issues should be explored in future research and ideally followed by a prospective multicentre study to optimise premedication for AER. Based on the variation in care in this study in terms of analgesic premedication there is scope to unify practice at centres providing AER for intussusception.

This study has some limitations. While conducted at a large Australian centre over two years, the number of AERs and in particular sedation used is limited. This small sample size does not allow firmer statements on the safety of periprocedural analgesia and sedation for AER and any association between these practices and the outcomes of AER. Ideally sedation and pain scores would have been recorded. As a retrospective study, our findings are limited by the accuracy and quality of the data

entered into the EMR by both clerical and clinical staff. We have attempted to follow best practice for chart reviews²⁰ by formulating an explicit study protocol with predetermined inclusion and exclusion criteria, a clear definition of variables based upon literature review, a standardised data abstraction form on REDCap to allow uniform data handling of conflicting, ambiguous, missing or unknown data.

CONCLUSION

The use of periprocedural analgesia for AER in this Australian series was common, whilst sedation use was infrequent. Despite historical concerns that suppressing the pain or sedating a child with intussusception may worsen their outcomes of AER, our current practice reflects a high rate of successful AER without significant complications, e.g. bowel perforations and sepsis. Our findings supplement other emerging evidence supporting consideration of routine periprocedural analgesia for children requiring AER for intussusception to improve periprocedural pain management and a reduce variation of care.

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Table 1: Demographics and Presentations

<i>Variable</i>	<i>n</i>	<i>Percentage %</i>
	73	
Demographics:		
Male	41	56.2
Age (months)	Mean 23 months (range 2-103)	
Presentations:		
First time	64	87.7
Location:		
Ileocolic	53	72.6
Not specified	7	9.6
Ileocaecal	6	8.2
Ileoileal	5	6.8
Colocolic	2	2.7
Cause:		
Idiopathic	63	86.3
Lead Point	10	13.7
Lymphoid Hyperplasia	6	
Duplication Cyst	2	
Meckel's Diverticulum	1	
Appendix	1	
Average duration of symptoms (days)	1.8 (range 0.1-10)	
Symptoms		
Abdominal Pain	61	83.5
Vomiting	38	52.1
Pulling up legs	33	45.2
Lethargy	23	31.5
Per Rectum bleeding	19	26
Pallor	16	21.9
Fever	10	13.7
Palpable Mass	10	13.7
Peritonism	2	2.7
Sepsis	1	1.4
Investigations		
Ultrasound	73	100
Blood Tests	57	78
Plain X Ray abdomen	11	15
Computed tomography abdomen	1	1.4

Table 2: Periprocedural Treatment

<i>Treatment</i>	<i>n</i>	<i>Percentage %</i>	<i>Dose range (per dose)</i>
Any analgesia	61	83.5	
Simple Analgesia (<4 h of AER)	28	38.4	
• Paracetamol	28	38.4	10-15mg/kg
• Ibuprofen	10	13.7	5-10mg/kg
• Paracetamol + codeine	Nil		
Opioid Analgesia (<2h of AER)	48	65.8	
• IV Morphine	41	56.1	0.1-0.2 mg/kg
• IN Fentanyl	9	12.3	1-1.5mcg/kg
• IV Fentanyl	8	11	1-2mcg/kg
• Oral Oxycodone	2	2.7	0.1-0.2mg/kg
Sedation (<1h of AER)	8	11	
• Midazolam IN/buccal	7	9.5	0.3-0.6mg/kg
• Propofol	2	2.7	2-2.3mg/kg
• Ketamine IV	1	1.4	2mg/kg
• Nitrous Oxide	1	1.4	70%
Antibiotics	48	65.8	
• 3 rd generation cephalosporins	45	61.6	
• Metronidazole	41	57.2	
• Ampicillin	1	1.4	
• Amoxicillin	1	1.4	
• Gentamicin	1	1.4	
• Benzylpenicillin	Nil		
IV Fluids	66	90.4	

AER air enema reduction

IV intravenous

IN intranasal

Table 3: Management and Outcomes of Intussusception

<i>Management and Outcomes</i>	<i>n</i>	<i>% (95% CI)</i>	<i>n</i> <i>(Analgesia)</i>	<i>n</i> <i>(Sedation)</i>
Spontaneous resolution (not requiring AER)	13/73	17.8 (9.0-26.6)	8/13	nil
Underwent AER	60/73	82.1 (73.3-90.1)		
Attempts:				
1	47/60	78.3	37/47	6/47
2	5	8.3	5/5	1/5
3	3	5.0	3/3	0/3
>3	5	8.3	5/5	1/5
Successful reduction via primary AER	54/60	90.0 (82.4-97.6)	44/53	6
Failed reduction via AER	6/60	10.0 (2.4-17.6)	6/6	1
Complications				
Number requiring surgery	7/60	11.7 (3.6-19.8)	7/7	1
Bowel resection	5	6.8		
Stoma formation	Nil			
Perforation	Nil			
Recurrence within 48 hours of AER	6	10 (2.4-7.6)	6	nil
Total number of patients with complications	12/73	16.4	12	1
Overall successful resolution of intussusception not requiring surgery	66/73	90.4 (83.6-97.1)	52	6

AER air enema reduction

CI confidence interval