Reduction of ileocolic intussusception under sedation or anaesthesia: a systematic review of complications

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ABSTRACT

Background Despite the increased use of sedation in children undergoing stressful procedures, reduction of ileocolic intussusception (RII) is usually performed on awake children without any form of sedation.

Objective To evaluate the incidence of severe complications of RII under sedation or anaesthesia.

Design A systematic review including English language original articles of any date.

Patients Children undergoing RII (pneumatic or hydrostatic) under sedation or anaesthesia.

Data sources Ovid Embase, Scopus, PubMed, the Cochrane Database of Systematic Reviews and the internet search engine Google Scholar.

Data extraction Three authors independently reviewed each article for eligibility. The Newcastle-Ottawa Scale was used to assess the quality of included studies.

Main outcome measures The primary outcome was the incidence of intestinal perforation during RII. The secondary outcomes were the incidence of sentinel adverse events defined as death, cardiopulmonary resuscitation, permanent neurological deficit and pulmonary aspiration syndrome.

Results The search yielded 368 articles. Nine studies with 1391 cases were included in the analysis. Of the nine studies, six had a score of ≤6 stars in the Newcastle-Ottawa Scale assessment, indicating low-to-moderate quality. Propofol-based sedation was used in 849 (59.2%) cases; 5 (0.6%) had intestinal perforation. Intestinal perforation was not reported in patients who were sedated with other sedatives. One patient had pulmonary aspiration syndrome.

Conclusions Although caution remains warranted, current data suggest that the incidence of severe complications due to RII under sedation or anaesthesia is low. Due to the lack of prospective data, it is difficult to ascertain the exact incidence of severe complications.

What is already known?

- Despite the increased use of sedation in children undergoing stressful procedures, reduction of ileocolic intussusception is usually performed on awake children without any form of sedation.
- One justification for not sedating these patients is the belief that sedation may increase the risk for intestinal perforation.
- Another possible justification is the risk of sedation adverse events.

What this study adds?

- Low rates of intestinal perforation and only one sentinel adverse event were found in this systematic review, suggesting that the incidence of severe complications is low.
- The lack of prospective studies limits the interpretation of our data.

INTRODUCTION

With a yearly incidence of approximately 56/100 000, ileocolic intussusception is an important cause of intestinal obstruction in infants.[1] The treatment of ileocolic intussusception is pneumatic or hydrostatic reduction under fluoroscopy or sonographic guidance, both distressing procedures. However, reduction of ileocolic intussusception (RII) is usually performed on awake children without any form of sedation. In the USA, it is estimated that only about 7% of children with intussusception are treated with sedation during RII.[2 3] In colonoscopy, by example, in which the bowel is also distended with gas, children experience high levels of discomfort and require deep sedation for the procedure.[4]

A possible justification against the use of sedation is the assumption that Valsalva manoeuvre protects against intestinal perforation during the procedure.[5 6] It is postulated that during air enema, the presence of Valsalva manoeuvre increases intracolonic pressure and reduces the risk of perforation. This theory is based on a single in vitro study of juvenile pigs.[6] Another possible justification is the risk of sedation adverse events in paediatric gastroenterology procedures.[7]

The objective of this systematic review was to identify all published reports of RII performed under sedation or anaesthesia and to evaluate the incidence of intestinal perforation, and severe complications related to the procedure or the sedation/anaesthesia.

METHODS

The review follows the recommendations made in the Preferred Reporting Items for Systematic Reviews and Meta-Analyses statement.[8] A protocol was written before the beginning of the study. The study was registered with the International Prospective Register of Systematic Reviews (PROSPERO) at https://www.crd.york.ac.uk/PROSPERO/ under registration number CRD42020220694.

Types of studies

We included original research studies of any date in which sedation/anaesthesia was performed on

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children undergoing RII. Studies were included whether or not they compared sedation with non-sedation. The patients included in the analysis were only those who underwent sedation. Studies were excluded if they were editorials, survey studies or reviews. Case series and case reports were included in the analysis. We excluded studies that were not in English, and studies in which sedation or anaesthesia was provided only to patients who failed the first reduction attempt. We also excluded studies that were conducted in limited-resource settings. In these settings, many patients present >48 hours after the onset of symptoms and therefore may be more severely ill at presentation.[9]

Types of interventions and patients

We included any type of RII, pneumatic or hydrostatic, that were performed in any department clinic, or the operating room. Children aged 0–18 years were included.

Types of medications

All types of medications used for mild sedation, moderate sedation, deep sedation or general anaesthesia were included. Opioid medications were not included. Drugs given alone or in combination, as intravenous or intramuscular injection, inhalational, oral and intranasal were included.

Search strategy

A senior expert librarian designed and conducted a comprehensive search of electronic databases, including Ovid Embase, Scopus, PubMed and the Cochrane Database of Systematic Reviews. The Medline search strategy is included in online supplemental appendix 1. The internet search engine Google Scholar was searched using the search terms "intussusception" and "reduction" and "paediatric" OR "pediatric" and "sedation" OR "anaesth" OR "anesth" to identify articles published in electronic journals, books and scientific websites. We also completed a hand search of references of included studies.

Study selection

The review process had two steps. First, all articles yielded by the search were reviewed by three authors independently (MG, SG, RJ). Once this step had been completed, the three authors met with the lead author (IS), and any disagreement was resolved by consensus.

Data extraction

Data were extracted independently by the three authors (MG, SG, RJ) using a standardised data form. Data collection included study design, patients' age, medications administered, total number of procedures performed, rates of successful reductions, bowel perforations, any complications and sedation/anaesthesia-related adverse events. The extracted data were compared between the three reviewers, and discrepancies were resolved through discussion.

Outcome measures

The primary outcome was intestinal perforation during RII. The secondary outcome were sentinel adverse events reported according to a consensus document from the International Sedation Task Force of the World Society of Intravenous Anesthesia.[10] Sentinel adverse events were defined as death, cardiopulmonary resuscitation (CPR), permanent neurological deficit and pulmonary aspiration syndrome (known or suspected inhalation of foreign material such as gastric contents into the respiratory tract associated with new or worsening respiratory signs).[10] We contacted authors by email to verify that no data on adverse events were missing. There were no instances of missing information for these data extraction points.

Assessment of methodological quality of included studies

We used the Newcastle-Ottawa Scale, a tool adapted from previous systematic reviews to assess the quality of non-randomised studies in emergency medicine. The Newcastle-Ottawa Scale is a quality assessment tool used to evaluate non-randomised studies based on an eight-item score divided into three domains. These domains assess the quality of selection of study participants, comparability and ascertainment of the outcome of interest.[11–13]

Data analysis

Quantitative data were summarised by medians and means, and categorical data were summarised by numbers and percentages.

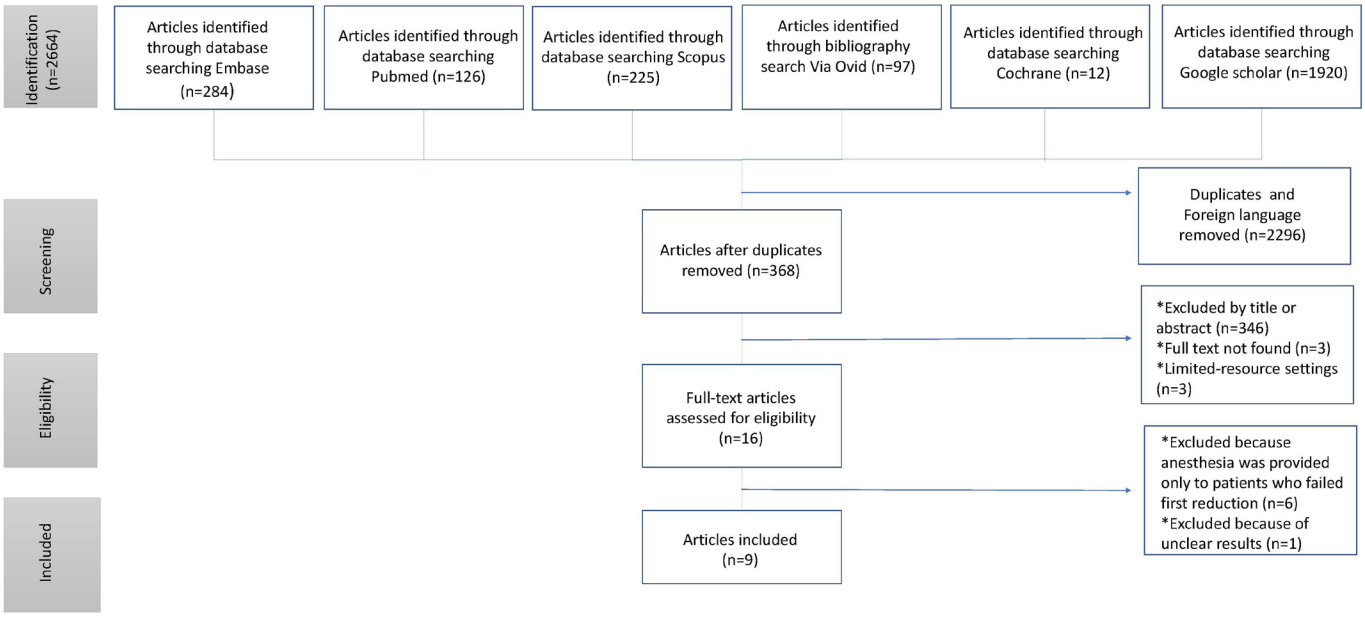

Figure 1 Preferred Reporting Items for Systematic Reviews and Meta-Analyses flow diagram.

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Table 1 Characteristics and results of included studies

Study	Country	Setting	Number of cases	Age (months)	Reduction procedure	Medications	Rate of successful reduction (%)	95% CI (%)	Intestinal perforation cases reported	Sentinel adverse events*
Roik *et al*[22]	Poland	Radiology Department	27	Mean=31 SD not reported	Hydrostatic	Chloral hydrate 50 mg/kg (per rectum)	23/27 (85.1)	67.5 to 94.1	None	
Ilivitzki *et al*[23]	Israel	Radiology Department	131	Not reported	Pneumatic	Propofol 1 mg/kg	121/131 (92.4)	86.5 to 95.8	2	
Purenne *et al*[24]	France	Operating room	337	Median=15 IQR not reported	Pneumatic	Intravenous flunitrazepam or midazolam +atropine	285/337 (85)	80.3 to 88.0	None	One case of pulmonary aspiration; 9-month-old infant who received midazolam, with no deleterious consequences
		Operating room	172	Median=17 IQR not reported	Pneumatic	Induction: propofol 4–6 mg/kg+succinylcholine 1.5–2 mg/kg, tracheal intubation; maintenance with propofol doses or sevoflurane 0.5–1 MAC	155/172 (90)	84.7 to 93.7	None	
Esposito *et al*[25]	Italy	Radiology Department	144	Mean=14 SD not reported	Hydrostatic	Midazolam 0.5 mg/kg (maximum 15 mg) oral or intranasal +ranitidine and betamethasone	122/144 (85)	78.0 to 89.7	None	
van de Bunt *et al*[26]	The Netherlands	Radiology Department	20	Mean=16 SD not reported	Hydrostatic	Ketamine 0.5–1 mg/kg+atropine 0.01 mg/kg	18/20 (90)	69.9 to 97.2	None	
Feldman *et al*[27]	Israel	Radiology Department	124	Mean=14.7 SD=10.2	Pneumatic	Propofol loading bolus dose of 1 mg/kg or in combination with ketamine 1 mg/kg, midazolam 0.1–0.2 mg/kg or fentanyl 1–1.5 µg/kg, followed by propofol boluses of 0.5 mg/kg every 1–2 min	117/124 (94.4)	88.8 to 97.2	3	
Shavit *et al*[28]	Israel	Radiology Department	14	Median=11 IQR=6–20	Pneumatic	Ketamine 1 mg/kg+propofol 1 mg/kg (8 patients); ketamine 2 mg/kg (5 patients), midazolam 0.1 mg/kg+ketamine 1 mg/kg (1 patient)	14/14 (100)	–	None	
Yeoh *et al*[29]	Australia	Radiology Department	8	Not reported	Pneumatic	Midazolam intranasal/buccal 0.3–0.6 mg/kg or propofol 2–2.3 mg/kg or ketamine intravenous 2 mg/kg, or nitrous oxide 70%	8/8 (100)	–	None	
Sacks *et al*[30]	Israel	Operating room	414	Median=8 IQR=5–12	Hydrostatic	Propofol 2 mg/kg	356/414 (85.9)	82.3 to 89.0	None	

*Sentinel adverse events were defined as death, cardiopulmonary resuscitation, permanent neurological deficit and pulmonary aspiration syndrome.[10]

Table 2 Quality assessment of included studies using the Newcastle-Ottawa Scale[11]

		Selection					Outcome			
Study	Design	Representativeness of the exposed cohort	Selection of the non-exposed cohort	Ascertainment of exposure	Demonstration that outcome of interest was not present at start of study	Comparability	Assessment of outcome	Was follow-up long enough for outcomes to occur	Adequacy of follow-up of cohorts	Overall quality
Roik *et al*[22]	Retrospective cohort	1	0	1	0	0	1	1	1	5
Ilivitzki *et al*[23]	Retrospective cohort	1	0	1	0	0	1	1	1	5
Purenne *et al*[24]	Retrospective cohort	1	1	1	0	1	1	1	1	7
Esposito *et al*[25]	Retrospective cohort	1	1	1	0	1	1	1	1	7
van de Bunt *et al*[26]	Retrospective case-control	1	1	1	0	1	1	1	1	7
Feldman *et al*[27]	Retrospective cohort	1	0	1	0	1	1	1	1	6
Shavit *et al*[28]	Prospective case series	1	0	1	0	0	1	1	1	5
Yeoh *et al*[29]	Retrospective cohort	1	0	1	0	0	1	1	1	5
Sacks *et al*[30]	Retrospective cohort	1	0	1	0	0	1	1	1	5

Study, patient and treatment-level data were summarised using basic descriptive statistics. The Wilson score interval was used for estimating the binomial proportion CI.

RESULTS

The systematic search yielded 368 papers, of which 16 were eligible for full-text assessment (figure 1). Six were excluded: one because of unclear results ('manipulation on 75% of the patients receiving midazolam'),[14] and six because the sedative medications were administered only to patients who failed the first reduction attempt.[15–20] We also excluded a paper from 1975 in which the phrase 'general anaesthesia induced by mask' was used without specifying the anaesthetic medication.[21] No perforation or sentinel adverse event were reported in the excluded studies.

Description of included studies

Nine studies with 1391 cases (786 pneumatic reductions and 605 hydrostatic reductions) were included in the final analysis; one prospective case-series study, one retrospective case-control study and seven retrospective cohort studies.[22–30] Of the nine studies, four were from Europe (Italy, France, The Netherlands and Poland), four were from Israel and one from Australia (table 1). There were no studies from North America or from the UK. Propofol-based sedation/anaesthesia was used in 849 (59.2%) cases. Additionally, a variety of other sedative and anaesthetic agents were used: oral and intranasal midazolam; rectal chloral hydrate; intravenous midazolam; intravenous ketamine/esketamine; inhalation of nitrous oxide, inhalation of sevoflurane. In one study, patients underwent tracheal intubation for the procedure.[24]

Quality assessment of included studies

Of the nine studies, six had a score of ≤6 stars in the Newcastle-Ottawa Scale assessment, indicating a low-to-moderate quality (table 2).[11]

Intussusception reduction rates

The total reduction success rate under sedation/anaesthesia was 1247/1434 (86.9%). Propofol-based sedation/anaesthesia had a success rate of 757/849 (89.2%).

Intestinal perforation rates

Intestinal perforation was reported only in 5/849 (0.6%) reductions under propofol-based sedation/anaesthesia (table 1). In

Table 3 Characteristics of five patients who underwent intestinal perforation during reduction of intussusceptions

Study	Age (months)	Symptom duration prior to ED arrival (hours)	Reduction procedure	Medication	Perforation location	Surgical treatment	Outcome
Ilivitzki *et al*[23]	Not reported	48	Pneumatic	Propofol	Not reported	Manual reduction of intussusception; suturing of perforation	Complete recovery
	Not reported	48	Pneumatic	Propofol	Not reported	Manual reduction of intussusception; suturing of perforation	Complete recovery
Feldman *et al*[27]	5	>24	Pneumatic	Propofol	Ascending colon	Resection of ischaemic bowel with primary anastomosis	Complete recovery
	6	>24	Pneumatic	Propofol	Cecum	Manual reduction of intussusception; suturing of perforation	Wound infection and abdominal fluid collection; needed surgical drainage; fully recovered and discharged after 13th hospitalisation day
	3	>12	Pneumatic	Propofol	Transverse column	Suturing of perforation	Uneventful after 8 days of hospitalisation

ED, emergency department.

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four of these five patients, the symptoms of intussusception began >24 hours before the reduction (table 3).

Sentinel adverse events

No case of death, CPR or permanent neurological deficit were reported; 1/1434 (0.07%) 9-month-old who was sedated with intravenous midazolam had pulmonary aspiration syndrome (table 1).

DISCUSSION

This is the first systematic review that summarised the evidence on RII under sedation or anaesthesia in children. We found that the incidence of intestinal perforation was 0.6%, and only one (0.07%) patient had sentinel adverse event (pulmonary aspiration syndrome). No patient died, underwent CPR or suffered from permanent neurological deficiency. The lack of prospective studies limits the interpretation of our data to a certain extent; however, our data seem to suggest that sedation can be safely performed in these patients. One justification for not sedating these patients has been the belief that sedation may increase the risk for perforation.[6 31] A previous review reported that children undergoing RII have a perforation rate of 0.8%.[32] Other studies reported an estimate of perforation rate for pneumatic reduction of 0.3%–0.4%.[33 34] The patients included in these studies were not sedated for the procedure.[32–34] The 0.6% incidence for perforation found in the current review is consistent with the range reported in these studies, and suggests that sedation/anaesthesia is not associated with an increased risk for intestinal perforation.

In three cases, the patient was younger than 6 months of age and in four of the five cases symptoms of intussusception began >24 hours before emergency department arrival (table 3). These findings suggest that younger age and prolonged symptomatology prior the reduction increase the risk of perforation. Our findings are corroborated by similar observations from a previous study.[35]

Another rationale for not sedating children is that doing so would decrease the success of the reduction rate.[36] In a comprehensive meta-analysis, which included 32 451 children, pneumatic reduction and hydrostatic reduction had success rates of 82.7% and 69.6%, respectively.[33] The findings of the current review show an overall success rate of 86.9% under sedation, and a success rate of 89.2% for propofol-based sedation, suggesting that the success rate of reduction under sedation/anaesthesia is as high as the success rate of reduction without sedation/anaesthesia.

Our search did not identify any article from the USA or from the UK. A possible explanation is the low rates of RII under sedation or anaesthesia in these countries.[31 36]

This review has several limitations. First, there was heterogeneity regarding medication regimen. Second, we selected the Newcastle-Ottawa Scale which is most comprehensive in assessing the quality of non-randomised trials, this assessment scale has been criticised for being difficult to apply.[37] Third, we were unable to examine the recurrence rate of intussusception as these data were not reported. Fourth, we could only access occurrences of intestinal perforation and sentinel adverse events reported in the medical literature, and thus cannot exclude the possibility of intestinal perforation or severe adverse events that went unreported in peer-reviewed journals.

CONCLUSIONS

This systematic review identified only few occurrences of intestinal perforation in children treated with sedation or anaesthesia for reduction of intussusception, and only one sentinel adverse event. Although caution remains warranted, current data suggest that the incidence of severe complications due to RII under sedation or anaesthesia is low. Due to the lack of prospective data, it is difficult to ascertain the exact incidence of severe complications.

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Contributors MG designed the study, analysed and interpreted the data, reviewed the literature and critically revised the article; SGS analysed and interpreted the data, reviewed the literature and critically revised the article; RJ analysed and interpreted the data, reviewed the literature and critically revised the article. DMC interpreted the data, reviewed the literature and critically revised the article. IS conceived the idea for the study, analysed and interpreted the data and drafted the manuscript. MG and IS have full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. All authors approved the final manuscript as submitted and agreed to be accountable for all aspects of the work.

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Patient consent for publication Not required.

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Provenance and peer review Commissioned; externally peer reviewed.

Data availability statement All data relevant to the study are included in the article or uploaded as supplementary information.

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