

# Comparing sedative and non-sedative reduction techniques in paediatric intussusception: Insights from a 6-year study

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## ABSTRACT

**Introduction:** Intussusception is a prevalent paediatric emergency condition. The standard of care involves the reduction using air or fluid enema is considered a safe procedure. Sedation-induced muscle relaxation thus optimising the treatment. We present a comprehensive 6-year study involving non sedative reduction (NSR) versus sedative reduction (SR) utilising ketamine and midazolam.

**Materials and Methods:** A retrospective cohort study was conducted between January 2017 and July 2023 in Yogyakarta, Indonesia. A total of 85 children diagnosed with intussusception underwent hydrostatic reduction, which employed water-soluble contrast administered into the rectum. Cases that were unsuccessful in reduction underwent immediate surgical intervention.

**Results:** Among the 85 children with intussusception underwent reduction, 22 children underwent the SR procedure and 63 underwent NSR procedure. We found a successful outcome in 17 cases (77%) of SR procedure with one recurrent and the other five (23%) got surgical reduction such as anastomosis resection (3 cases) due to Meckel-Diverticula. On the other hand, we found 24 successful cases (38.0%) in NSR procedure with one recurrent after case. 39 others who failed with NSR continued to surgical reduction. Manual reduction was done for 31 patients with one case mortality due to pulmonary bleeding. Anastomosis resection (4 cases) and, stoma (4 cases) were decided for others surgical reduction. The relative risk (RR) on this study was 2.02 (p value < 0.05, CI 95%).

**Conclusion:** Implementation of the SR procedure may reduce surgery rates in paediatric intussusception, thereby enhancing patient management. Furthermore, the success rate of hydrostatic reduction higher in under sedation procedure. We contribute to evolve insight of non-operative approaches of paediatric intussusception management, particularly in the Yogyakarta.

## KEYWORDS:

*Paediatric, intussusception, hydrostatic reduction, sedative*

## INTRODUCTION

Intussusception is a prevalent paediatric emergency condition and the main cause of bowel obstruction in children aged less than 5 years, which is an invasion of the proximal bowel into the distal bowel. The structures frequently involved in this condition are the small intestine and colon. Ileocolic intussusception is the most typical type of intussusception, with ileoileocolic, enteroenteric and colocolic intussusceptions occurring less frequently.<sup>1</sup> Its early identification and care are crucial because late diagnosis can result in ischemia, potentially leading to necrosis, perforation and peritonitis to death due to septic shock.<sup>2,4</sup> The best diagnostic method is transabdominal ultrasonography because of its high sensitivity (98%), safety and accessibility. The standard of care for intussusception involves the reduction using air or fluid enema is considered a safe procedure.<sup>4</sup> Hydrostatic reduction (HR) through the anorectal route offers a surgical risk-free alternative. While there has been ongoing debate regarding the efficacy of employing sedation, recent research has indicated that sedative reduction can be a successful method for treating intussusception. This may be attributed to its ability to induce smooth muscle relaxation, allowing healthcare providers to secure patient cooperation while minimizing movements and cries.<sup>5</sup> We present a comprehensive 6-year study involving non sedative reduction (NSR) versus sedative reduction (SR) utilising ketamine and midazolam.

## MATERIALS AND METHODS

### Patients and Methods

This research is a retrospective cohort study to compare the effectivity of non-sedative reduction (NSR) versus sedative reduction (SR) utilising ketamine and midazolam to reduce surgery rates in paediatric intussusception. A total of 85 children with intussusception with hydrostatic reduction were included in the study, conducted between January 2017 and July 2023 at Sardjito Hospital, Yogyakarta, Indonesia. Data included patient age, sex, body weight, vomiting, bloody stools, abdominal distention, symptom duration, location intussusception and recurrence of intussusception were collected and analysed during a retrospective chart review. Patients who had unstable hemodynamic, peritonitis, pneumoperitoneum at the time of their initial presentation

**Table I: Characteristic of children with intussusception in each treatment group**

| Characteristics                        | Treatment groups        |                             |  | p-value |
|--|-------------------------|-----------------------------|--|---------|
|  | Sedative<br>(mean ± SD) | Non-sedative<br>(mean ± SD) |  |         |
| Age (mo)                               | 25 ± 14.38              | 17.14 ± 12.29               |  | 0.136   |
| Weight (kg)                            | 11.38 ± 4.45            | 9.08 ± 2.39                 |  | 0.012*  |
| Duration of clinical manifestation (h) | 80.57 ± 41.42           | 75.27 ± 42.21               |  | 0.765   |

|                          | Sedative |      | Non-sedative |      | p-value |
|--------------------------|----------|------|--------------|------|---------|
|                          | n        | %    | n            | %    |         |
| Gender                   |          |      |              |      | 0.459   |
| Male                     | 12       | 54.5 | 40           | 63.5 |         |
| Female                   | 10       | 45.5 | 23           | 36.5 | 0.459   |
| Clinical manifestation   |          |      |              |      |         |
| Vomiting                 | 21       | 95.5 | 50           | 79.4 | 0.08    |
| Red currant jelly stools | 12       | 54.5 | 39           | 61.9 | 0.544   |
| Abdominal distension     | 8        | 36.4 | 27           | 42.9 | 0.594   |
| Location                 |          |      |              |      | 0.07    |
| Right                    | 14       | 63.6 | 26           | 41.3 |         |
| Left                     | 8        | 36.4 | 38           | 58.7 |         |

**Table II: Comparison of reduction successful rate between groups**

|           |              | Reduction successful rate |      |        |      |       |     | p-value | RR    | 95% Confident interval |
|-----------|--------------|---------------------------|------|--------|------|-------|-----|---------|-------|------------------------|
|           |              | Success                   |      | Failed |      | Total |     |         |       |                        |
|           |              | n                         | %    | n      | %    | n     | %   |         |       |                        |
| Procedure | Sedation     | 17                        | 77.3 | 5      | 22.7 | 22    | 100 | 0.002   | 2.028 | 1.376 – 2.990          |
|           | Non sedation | 24                        | 38.1 | 39     | 61.9 | 63    | 100 |         |       |                        |
|           | Total        | 41                        | 48.2 | 44     | 51.8 | 85    | 100 |         |       |                        |

underwent immediate surgery and were not included in this study.

A supine position was used to perform hydrostatic reduction on the patient, and water-soluble contrast was inserted through an anorectal tube at the level of 1 meter of hydrostatic pressure. The radiologist monitored the passage of fluid through the intussusception under fluoroscopy guiding. Ketamine (1 mg/kg/dose) and midazolam (0.1 mg/kg/dose) were delivered intravenously 5 minutes prior to the attempt at hydrostatic reduction in the patient undergoing the SR procedure. Throughout the procedure, the patient's state of consciousness, breathing rate, heart rate and blood oxygen levels were closely observed due to the potential risk of apnoea or respiratory cessation. If the chosen approach proved ineffective, prompt surgical intervention under general anaesthesia was pursued following the acquisition of written informed consent.

**Statistical Analysis**

SPSS 26.0 for Windows (IBM, Chicago, IL, United States) was used for the statistical analysis. Patients were divided into two groups who underwent SR procedure (SR group) and NSR procedure (NSR group). Data were expressed as mean ± standard deviation or number and percentage. Chi-square test was used to analyse risk factors contributing to HR failure. Statistical significance was set as p value < 0.05. We analyse the risk estimate between two groups.

**RESULTS**

The mean age of the patient was 25 ± 14.38 months in the SR group and 17.14 ± 12.29 months in the NSR group, the mean weight was 11.38 ± 4.45 kg and 9.08 ± 2.39 kg in SR groups and NSR groups respectively. The mean duration of clinical manifestations was 80.57 ± 41.42 and 75.27 ± 42.21 hours in the SR group and NSR group respectively. Most of the children in both groups were male, 12 (54.5%) and 40 (63.5%). Vomiting, bloody stools and abdominal distension were observed in 21 (95.5%), 12 patients (54.5%) and eight (36.4%) patients in the SR group respectively. In the NSR group, vomiting, bloody stools and abdominal distension were observed in 50 (79.4%), 39 patients (61.9%) and 27 (42.9%) patients. Based on the location of the abnormalities, in the SR group most (63.6%) of the abnormalities occurred in the right side of intestine, while in the NSR group, most of the abnormalities were located in the left side of intestine, namely in 38 patients (58.7%) (Table I).

In this study, among 85 children with intussusception who underwent hydrostatic reduction, 22 children underwent the SR procedure and 63 underwent the NSR procedure. Among 63 children who underwent the NSR procedure, we found 24 successful cases (38.0%) of the NSR procedure with one recurrent after case. 39 others who failed with NSR continued to surgical reduction. Manual reduction was done for 31 patients with one case of mortality due to pulmonary bleeding. Anastomosis resection and stoma were performed in each of the other four patients. On the other hand, in the

Table III: Baseline characteristics of children with EA in our institution

| Characteristics  | n (%)     |
|--|-----------|
| Sex  |           |
| • Male   | 28 (52.8) |
| • Female   | 25 (47.2) |
| Weight at diagnosis (gram)                                       |           |
| • Normal weight ( $\geq 2500$ )                                  | 22 (41.5) |
| • Low weight ( $< 2500$ )  | 28 (52.8) |
| • Very low weight ( $< 1500$ )                                   | 3 (5.6)   |
| • Extremely low weight ( $< 1000$ )                              | 0         |
| Gestational age  |           |
| • Preterm  | 15 (28.3) |
| • At term  | 11 (20.8) |
| • Post-term  | 27 (50.9) |
| EA type  |           |
| • Isolated EA without TEF (Gross A)                              | 9 (17)    |
| • EA with distal TEF (Gross C)                                   | 44 (83)   |
| Thrombocytopenia ( $< 150,000/\text{mm}^3$ )                     |           |
| • Yes  | 31 (58.5) |
| • No   | 22 (41.5) |
| Pneumonia  |           |
| • Yes  | 48 (90.6) |
| • No   | 5 (9.4)   |
| Sepsis   |           |
| • Yes  | 50 (94.3) |
| • No   | 3 (5.7)   |
| Definitive surgery (oesophageal anastomosis)                     |           |
| • Yes  | 17 (32.1) |
| • No   | 36 (67.9) |
| Outcome  |           |
| • Survived   | 10 (18.9) |
| • Died   | 43 (90.1) |
| Associated anomaly   |           |
| • VACTERL  | 27 (51)   |
| • VACTERL, undescended testis                                    | 1 (1.9)   |
| • VACTERL, Opitz G/BBB syndrome                                  | 1 (1.9)   |
| • VACTERL, Down syndrome, clubfoot                               | 1 (1.9)   |
| • VACTERL, Meckel diverticulum                                   | 1 (1.9)   |
| • VACTERL, hypospadias, undescended testis, left radial clubhand | 1 (1.9)   |
| • VACTERL, dextrocardia  | 2 (3.8)   |
| • VACTERL, cholestasis   | 1 (1.9)   |
| • Tracheomalacia   | 1 (1.9)   |
| • No associated anomaly  | 14 (26.4) |
| • Unknown  | 3 (5.7)   |

EA: Oesophageal atresia; TEF: Tracheoesophageal atresia

Table IV: Multivariate analysis of survival of children with EA in our institution

| Variables            | HR (95% CI)       | p-value |
|----------------------|-------------------|---------|
| Sex                  | 0.82 (0.42–1.63)  | 0.578   |
| EA type              | 0.69 (0.23–2.02)  | 0.496   |
| Thrombocytopenia     | 2.67 (1.22–5.85)  | 0.014*  |
| Pneumonia            | 3.67 (0.84–16.04) | 0.084   |
| Sepsis               | 0.80 (0.12–5.41)  | 0.817   |
| Definitive treatment | 0.39 (0.17–0.87)  | 0.022*  |

\*,  $p < 0.05$ ; CI: Confidence interval; HR, hazard ratio; EA, oesophageal atresia

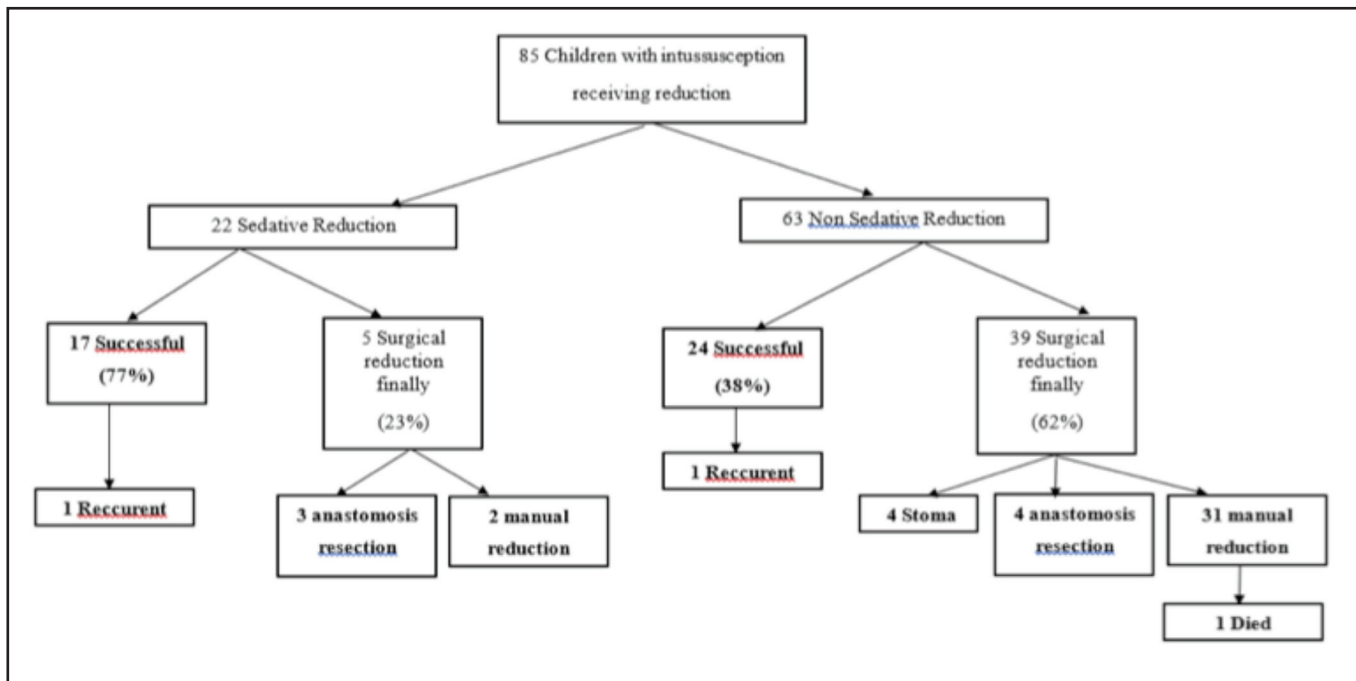


Fig. 1: Flow chart of management results for children with intussusception underwent hydrostatic reduction with or without SR procedure

22 children who underwent the SR procedure, we found a successful outcome in seventeen cases (77%) of the SR procedure with one recurrent. The other five (23%) got surgical reduction such as anastomosis resection(3 cases) due to Meckel-Diverticula (Figure 1).

Based on the results of the study, successful outcome of the procedure was found in 17 cases (77%) of the SR group and 24 successful cases (38%) in the NSR group. The results of this study indicate that there is a significant difference in the reduction successful rate between the SR and NSR groups. The relative risk (RR) was 2.028 (p value = 0.002, 95% CI: 1.376 – 2.990) (Table II).

**DISCUSSION**

Intussusception is a common aetiology of acute abdominal conditions in paediatric patients. The worldwide average annual incidence ranges from 0.24 to 2.4 cases per 1000 live births, with an approximate male-to-female ratio of 2:1, with a significant occurrence in boys. Paroxysmal stomach discomfort, vomiting, red currant jelly stools and a palpable abdominal mass are among the classical symptoms and warning indicators.<sup>6</sup> In this study, we observed vomiting, red currant jelly stools and abdominal distension were in 21 (95.5%), 12 patients (54.5%) and eight (36.4%) patients in the SR group respectively. In the NSR group, vomiting, red currant jelly stools and abdominal distension were observed in 50 (79.4%), 39 patients (61.9%) and 27 (42.9%) patients. The clinical manifestation of intussusception varies between patients. Only 20% of cases have the classical clinical presentation, which includes stomach pain, vomiting, bloody stools and an abdominal mass. In addition, most children do not exhibit the whole symptom triad of abdominal pain,

vomiting and bloody stools. Vomiting, irritability, fatigue, or bloody stools tend to be more prevalent among younger children, while older children commonly present with stomach pain. The clinical manifestation of intussusception aligns with the patient's age. It is imperative to underscore that these various characteristics, when observed, should heighten clinical suspicion for intussusception to ensure that infants with nonspecific symptoms receive a proper diagnosis.

Infant intestinal obstruction is frequently caused by ileocolic intussusception in order to avert the grave complications of intestinal necrosis, perforation, peritonitis, shock and potential fatality, it is imperative to swiftly and efficiently address intussusception. The established approach for managing intussusception is pneumatic reduction of intussusception (PRI) with fluoroscopic guidance, which entails the introduction of a catheter into the colon and inflation to a pressure range of approximately 80 to 100 mm Hg. Other therapeutic choice is hydrostatic reduction with normal saline or water-soluble contrast. Despite the fact that there aren't any studies that have examined discomfort during reduction yet, deep sedation is frequently used during colonoscopies, which is analogous. Recent investigations have shown the efficacy of reduction when anaesthesiologists provide the sedation. However, in most institutions, reduction is carried out on awake children without sedation.<sup>9</sup>

In this study we found that there are significant reduction successful rate differences between SR procedure and NSR procedure. The percentage of successful reduction rate in SR group is higher than NSR (RR 2.028 (95% CI 1,376 – 2.990; p = 0.002). The findings of this investigation align with those of Doo and Kim (2020), who reported a 65.1% success rate in

the performance of SR in 43 patients over a 3-year period. The achievement of successful reduction can be reliably facilitated by employing the SR procedure in conjunction with intravenous administration of ketamine, midazolam and atropine. This approach holds promise for reducing the necessity for surgical interventions in cases of paediatric intussusception.<sup>10</sup>

The findings of this study are consistent with previous study<sup>12</sup>. In their study, they conducted a total of 38 reductions, involving 31 patients and seven cases of recurrence. These reductions were performed using water under ultrasound guidance with sedation, resulting in a success rate of 76%. Importantly, no noteworthy adverse effects were documented in patients who underwent ultrasound-guided hydrostatic reduction under sedation. Notably, the success rate was notably higher in this particular group ( $p = 0.20$ ). Factors that appeared to correlate with the need for surgical intervention included a greater length of the intussusception ( $p = 0.03$ ), a location outside the right colon ( $p = 0.002$ ), and a longer duration between the onset of symptoms and diagnostic imaging tests ( $p = 0.08$ ). Poonai et al.<sup>14</sup> further supports the regular consideration of sedation in the case of children undergoing intussusception reduction. Importantly, it was established that the use of sedation did not exhibit any increased likelihood of adverse events (OR: 1.1; 95% CI: 0.6 2.1;  $p = 0.79$ ) or perforation (OR: 2.1; 95% CI: 0.7 6.9;  $p = 0.21$ ).<sup>3</sup>

The role of sedation in intussusception reduction remains a topic of ongoing investigation and debate. While certain studies have indicated lower success rates, others have reported a higher rate of achievement when sedation is employed. In our own clinical experience, we observed that in 10 to 14% of intussusception cases, which were initially unreducible by the radiology team and later assessed by the surgeon in the operating theatre after the administration of anaesthesia, the intussusception had resolved. This resolution was attributed to the beneficial effects of sedation, which promote muscle relaxation and reduce extraluminal abdominal pressure. These effects have been documented in prior research and are well-established in the field.<sup>12</sup> Fear and pain also can be reduced by using sedatives or anaesthetic during the enema treatment. Children have the ability to relax and work more cooperatively. A study found that applying midazolam to a small number of cases—just 16 in the atropine group and 16 in the control group increased the success rate of reduction from 68.8 to 93.8%.<sup>8</sup> Furthermore, a separate study demonstrated that deep sedation yielded comparable success rates to those achieved under general anaesthesia. The success of the reduction is also enhanced by employing the correct treatment and sedation regimen.<sup>13</sup>

In our investigation, the anaesthesiologist administered ketamine either as a standalone sedative or in conjunction with midazolam. Our study's findings find corroboration in the work of Shavit et al.,<sup>16</sup> who also employed the same sedation medication. The choice to utilise sedation based on ketamine appears suitable when considering the anaesthesiologist's familiarity with these drugs, the brief duration of the procedure, the necessity for immobilisation, the patient's age (over 3 months) and the discomfort

associated with the procedure.<sup>10,14</sup> According to the guidelines of the National Institute for Health and Care Excellence regarding sedation for paediatric procedures, options such as nitric oxide, ketamine combined with midazolam or fentanyl are typically recommended. Midazolam is often combined with other sedatives to best suit the clinical requirements. Ketamine has a well-established track record for safety and efficacy in inducing dissociative sedation, leading to a trance-like and cataleptic state, offering substantial pain relief, sedation, immobility and amnesia. Although it can occasionally result in issues like laryngospasm, ketamine generally maintains airway reflexes, cardiovascular stability and spontaneous respiration. Particularly when used in conjunction with midazolam, it significantly reduces the incidence of vomiting, shortens induction time and enhances parental satisfaction when compared to using ketamine alone.<sup>2,15,16</sup>

Hydrostatic reduction is the preferred treatment for intussusception unless it's not advisable. The failure rate of hydrostatic reduction is greater when the mass extends beyond the splenic flexure. However, it's important to note that in most cases where hydrostatic reduction fails, they can be easily resolved through laparotomy.<sup>17</sup> In our study, the hydrostatic reduction procedure couldn't be successfully carried out in 44 patients from both groups. This indicates that medical professionals may not prevent the possibility of perforation since an ischemic or necrotic intestinal wall is more susceptible to such an event. Nevertheless, even if a perforation occurs during the reduction process, it has minimal implications for subsequent medical care because surgery ultimately becomes necessary in cases of unresolved intussusception. There is a lesser chance of problems can be realised with increased case finding and faster management.<sup>7</sup>

This study is offering valuable insights. However, its limitations include a small sample size, especially in the sedative group, which might affect the reliability of the findings. Also, the uneven distribution of cases between sedative and non-sedative arms could impact of interpretation the results. Despite these limitations, the study emphasises the importance of exploring sedation reduction techniques to improve procedures for children and minimise trauma. Further research is needed to fully understand their impact on paediatric outcomes and well-being.

## CONCLUSION

The reduction successful rate of sedative procedure in hydrostatic reduction for children with intussusception is found to be higher than NSR procedure. Implementation of the SR procedure may reduce surgery rates in paediatric intussusception, thereby enhancing patient management. We contribute to evolve insight of non-operative approaches of paediatric intussusception management, particularly in Yogyakarta.

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