Sedative reduction method for children with intussusception

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Abstract
Intussusception is common emergency condition in children. Pneumatic or hydrostatic reduction (HR) is considered the first-choice management strategy in cases lacking indications for surgical intervention. Generally, sedatives are not used in children undergoing interventional radiology procedures. Surgical management is associated with long hospitalization durations and high costs, unlike nonsurgical reduction. To avoid surgery, reduction procedures are repeated despite initial treatment failure. However, in cases involving repeated failures, children should be referred for surgery.

To ensure good response to reduction, we planned HR under sedation during the third reduction attempt. Sedative reduction (SR) was performed with the administration of ketamine, midazolam, and atropine. All patients with contraindications against HR underwent laparoscopic reduction (LR) without HR.

During 3 years, SR was performed in 43 patients, and in 28 (65.1%), the treatment was successful. Among the 15 patients in whom the procedure failed, 14 underwent LR without intestinal resection. There was no significant risk factor contributing to failed reduction under sedation.

During the second or third HR attempt, successful reduction may be ensured with the SR procedure with intravenous ketamine, midazolam, and atropine; this procedure may further reduce surgery rates in pediatric intussusception.

Abbreviations: HR = hydrostatic reduction, LR = laparoscopic reduction, SR = sedative reduction.

Keywords: atropine, children, hydrostatic reduction, intussusception, ketamine, midazolam

1. Introduction
Intussusception is common cause of intestinal obstruction during childhood. Intussusception commonly occurs at the age of 1 year. If diagnosis and treatment are delayed, bowel necrosis, perforation, and even death due to septic shock may occur.

Pneumatic or hydrostatic reduction (HR) through anorectal enema is the treatment of choice because it avoids the risks associated with surgery, such as postoperative intestinal adhesion, longer hospitalization durations, and the resultant higher costs.[1,2]

In Korea, children with intussusception are usually transferred to a university hospital owing to the risk of perforation and necessity of surgery. If patients do not have any peritoneal irritation symptoms or perforation risk, pneumatic or HR is performed by a radiologist. If the initial attempt at reduction fails, a repeat procedure without sedation is preferred. However, in cases involving repeated failures, children should undergo surgical reduction. In our experience over several years, repeated non-sedative reduction (SR) procedures were ineffective. Therefore, we modified the nonsurgical reduction technique to one that involved the use of sedatives with smooth-muscle relaxants in patients with intussusception for whom repeated nonsurgical reduction attempts had failed.

2. Patients and methods
Between January 2016 and January 2019, 130 children diagnosed with intussusception in a single center were recruited for the present study. A retrospective chart review was performed, and data on patient age, sex, body weight, underlying disease, the symptoms of vomiting or bloody stool, symptom duration, and recurrence of intussusception were collected and analyzed. All patients were diagnosed with intussusception based on the confirmation of the target sign via abdominal ultrasonography or computed tomography. Patients who presented with signs of peritonitis, perforation, and hemodynamic instability, underwent surgery directly. If there were no contraindications
against nonsurgical reduction, patients underwent nonsedative HR, which was performed by an expert radiologist. In cases where the nonsedative approach failed repeatedly, we performed SR before switching to surgery after obtaining written informed consent. If the SR procedure failed, patients finally underwent laparoscopic reduction (LR) under general anesthesia. We analyzed the rates and factors of successful SR to determine the effectiveness of the procedure.

With the patient in a supine position, normal saline was administered through an inserted anorectal tube at the level of 1 m of hydrostatic pressure. The radiologist monitored the passage of fluid through the intussusception. If the patient cooperated well and the vital signs were stable, non-SR was attempted until the intussusception was reduced. In patients for whom the non-SR attempts failed twice, SR using ketamine (1 mg/kg/dose), midazolam (0.1 mg/kg/dose), and atropine (0.01 mg/kg/dose) was attempted in the same way. The drugs were administered intravenously 5 minutes before the reduction attempt. During the procedure, the patient’s level of consciousness, respiration rate, heart rate, and blood oxygen saturation were strictly monitored by a pediatrician owing to the risk of apnea or respiratory arrest. After 24 hours of successful reduction, abdominal sonography was performed again. If the SR procedure failed, patients were transferred to the operating room for surgery.

3. Statistical analysis

Statistical analysis was performed using SPSS 24.0 (IBM, Chicago, IL, United States) for Windows. Data were expressed as mean ± standard deviation or number and percentage. Chi-square test or Fisher exact test was used to analyze risk factors contributing to HR failure. Statistical significance was set at $P < 0.05$. Patients were divided into two groups after SR for comparing patients who underwent surgery (surgical group) and patients who did not undergo surgery (successful SR group). We analyzed risk factors for the failure of SR.

4. Results

The mean age of the patient cohort was 27.1 ± 18.5 months, and the mean weight was 12.9 ± 3.4 kg. The male to female ratio was 1.8:1. All patients had abdominal pain or irritability, which might be indicative of abdominal pain. Hematochezia and vomiting were observed in 28 (21.5%) and 37 patients (28.5%), respectively. Table 1 describes the risk factors contributing to failed reduction under sedation. We noted no significant differences in terms of risk factors between 28 successfully treated patients of SR group and 15 patients of final surgical group (Table 1).

Among 130 children with intussusception, we performed HR in 125 patients. Five patients underwent surgery because of contraindications against nonsurgical reduction. They showed the symptoms of peritoneal irritation, long-duration symptoms, or bowel perforation. Among the 125 patients who underwent HR, the first or second reduction attempt was successful in 82 patients (65.6%). One of the 82 patient experienced recurrence after successful reduction and underwent surgery. For 43 patients, nonsurgical reduction failed, and SR was chosen for the first nonsurgical attempt. In 28 patients (65.1%), SR successfully resolved symptoms. The 15 patients for whom SR failed, underwent LR (Fig. 1). Among these patients, only 1 child had spontaneous reduction while preparing for surgery. As a result, the HR was successful in 110 children (88.0%).

### Table 1

| Factors               | Success (n = 28) | Failure (n = 15) | $P$ |
|-----------------------|------------------|-----------------|-----|
| Sex (male, %)         | 17 (60.7%)       | 12 (80.0%)      | .203|
| Age, mo               |                  |                 |     |
| Over 12               | 19 (67.9%)       | 7 (46.7%)       | .112|
| Over 24               | 13 (46.4%)       | 4 (26.7%)       | .114|
| Weight (over 12 kg)   | 18 (64.3%)       | 6 (40.0%)       | .105|
| Symptoms              |                  |                 |     |
| Hematochezia          | 14 (50.0%)       | 9 (60.0%)       | .341|
| Vomiting              | 16 (57.1%)       | 6 (40.0%)       | .245|
| Duration of symptoms, h | 11 (39.3%)   | 9 (60.0%)       | .187|
| Over 24               |                  |                 |     |
| Over 48               | 4 (14.3%)        | 3 (20.0%)       | .721|
| Recurred intussusception | 8 (28.6%)   | 3 (20.0%)       | .512|

Mo = months, h = hours, HR = hydrostatic reduction.

5. Discussion

In the past few decades, many clinicians have studied intussusception reduction under general anesthesia, simple sedation, or other muscle relaxation. Franken et al. used intravenous glucagon as a smooth muscle relaxant during HR. However, the success rate of glucagon was same as the control group using placebo; thus, glucagon was not shown to be effective. In a study by Suzuki et al, reduction under general anesthesia did not improve the success rate of reduction.[3] They recommended that general anesthesia should not be used owing to its associated disadvantages. However, Purenne et al showed that the success rate of reduction under general anesthesia using propofol, succinylcholine, and sevoflurane was about 90% compared to 85% under sedation using midazolam and atropine.[4] Eisaour et al reported the success rate of reduction using midazolam to be 93.9%; however, the result was not statistically significant owing to the small sample size.[5] Although there are many controversies about the effectiveness of sedation or general anesthesia, recent studies showed that reduction under sedation or general anesthesia is effective.[6,7] In this study, SR using midazolam, ketamine, and atropine improved the success rate from 65.6% to 88.0%.

Vazquez et al suggested that external manual reduction under sedation with intravenous midazolam, ketamine, fentanyl, and atropine was effective; with this method, in 13 children, reduction was performed 15 times, and the reduction rate was 80%, nonsurgical reduction rate was 93%, and only 1 child underwent surgery.[7] However, the effectiveness and safety of this technique may be dependent on the clinician. Additionally, over-pressure can induce bowel perforation. Considering the risk-benefit of every treatment option mentioned above, we thought that sedative HR is more appropriate for children with intussusception. Comparing between HR under general anesthesia and sedation, general anesthesia required more steps, including consultations with anesthesiologists, preparation of operation rooms, and in some case, tracheal intubation. In contrast, preparing for SR was relatively easy and brief.

According to the National Institute for Health and Care Excellence guideline about infant sedation, in case of painful pediatric procedures, nitric oxide, ketamin with midazolam or fentanyl are usually recommended. Midazolam is generally used in combination with other sedative agents chosen to proper the
needs of the clinical condition. Ketamine has a strong safety and efficacy profile in enabling deep sedation and causes dissociative sedation, which creates a trance-like cataleptic state, with sedation, profound analgesia, immobility, and amnesia. Nevertheless, ketamine tends to preserve airway reflexes, cardiovascular stability, and spontaneous respiration; it occasionally can cause complications including laryngospasm. Especially in combination of ketamine and midazolam, it had significantly less vomiting, shorter induction time, and more satisfied parents compared to ketamine alone. However, there was more desaturation when using a combination of ketamine and midazolam for sedation. These can be both effects and adverse reaction or complication. We must administer the correct dose of drugs, and continuous monitoring of vital signs. Atropine acts as muscle relaxant by inhibiting the muscarinic actions of acetylcholine at postganglionic cholinergic nerves and smooth muscle. Using it, we can decrease gut motility and induce spontaneous resolving of intussusception.

In the pediatric radiologist survey, which included questions about the use of sedation, 93% of radiologists reported not using sedative procedures. In unsuccessfully reducted children, 64% wait and reattempt, 15% try again with positional change, and 19% apply manual pressure. About 20% try again for reduction after waiting 2 hours or more. Some radiologists were not in favor of SR because of the possibility of hidden symptoms of perforation during reduction. However, in our experience, there was no perforation during reduction under sedation because we ruled out the children with high risks of perforation such as delayed onset, having severe tenderness with rigid abdomen or remarkable rebound tenderness. Moreover, we set hydrostatic pressure strictly within 1 meter H2O. Most infants or younger children are irritable and cry during procedures, so it is not possible to observe children’s reaction for detection of perforation signs.

6. Conclusion

In Korea, pneumatic or HR without sedation is the first-choice treatment strategy for pediatric intussusception. Nonsurgical reduction is attempted two or three times to avoid surgery. In case of repeated failure, surgery is considered. Intravenous administration of ketamine, midazolam, and atropine can result in bowel relaxation in children with intussusception. This study has some limitations for single-institution study, small number of cases, and nonrandomized controlled trail design, SR using midazolam, ketamine, and atropine reduced surgery rates for pediatric intussusception cases from 36.9% to 15.4% for 3 years. In failed cases of this study, they showed irritability and poor cooperation. Sustained muscular contraction would have affected the failure of reduction. After sedation, reduction was successfully done. Under appropriate sedation, clinicians can achieve the patient’s cooperation and reduce the intestinal pressure and complication of pressure peaks by patient’s movement and crying.

Author contributions

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