



Overview on Gastrointestinal Foreign Bodies in Children

**Ahmed Abdelsamie Fadl^{a,b*#}, Asma Awad M. Alhazmi^{c≡},
Tariq Mohammed Alyami^d, Najla jaber Alkhaldi^e,
Abdulshaheed Salman Alhamdan^f, Waad Musayid Alsaedi^g,
Yazeed Nashi M. Alaufi^h, Meshary Saud Almotiryⁱ, Ashwaq Laili Alanazi^j
and Hussain Hassan Alrashdi^k**

^a Doctor Samir Abbas hospital, Saudi Arabia.

^b Department of Pediatrics, Al-Azhar university hospitals- Cairo, Egypt.

^c Umm Al Qura University, Saudi Arabia.

^d King Salman Hospital, Riyadh, Saudi Arabia.

^e Taif University, Saudi Arabia.

^f AlOmran General Hospital, Alhassa, Saudi Arabia.

^g Hera General Hospital, Makkah, Saudi Arabia.

^h Al-Rayan Colleges, Medina, Saudi Arabia.

ⁱ General Rumah Hospital, Saudi Arabia.

^j Imam Abdulrahman Bin Faisal University, Saudi Arabia.

^k General Muzailef hospital, Saudi Arabia.

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This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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Review Article

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ABSTRACT

Introduction: Greatest percentage of the upper gastro intestinal accidentally swallowed foreign bodies in adults are related to food bolus impaction with meat. Most patients who swallow a true foreign body typically are younger, however young children were recorded to accidentally swallow other objects rather than food poluses. Males are more often recorded, and often have significant

[#] Pediatric senior registrar;

[≡] Lecturer of pediatrics;

psychiatric illness and/or drug abuse. Foreign body (FB) ingestion is a very common problem in children. FB may pass through gastrointestinal (GI) system silently without any indication, or it may need an intervention to prevent complications. The diagnosis, decision for involvement and management may have some difficulties, and it's usually decided according to the case, especially in cases with protracted lodgment. Complications caused by lodgment of ingested GI FBs varies according to many factors and are associated with important morbidity and mortality in children.

Objectives: to show an overview of gastrointestinal foreign bodies in children, its epidemiology, risk factors, hazards and management.

Keywords: Foreign bodies; child; endoscopy.

1. INTRODUCTION

Management of accidentally foreign body ingestion in children (FBI) is considered one of the most challenging problems in pediatric medicine. The myriad differences in size, type, and timing of foreign object ingested, compounded by many patient factors, such as age, underlying medical issues, and clinical presentation, make each case inherently different than the each other. For example, Button battery (BB) ingestions (BBIs) epitomize the task of pediatric FBI, as the result can range from harmless to death. As the authors' center has personally experienced, when death occurs as a consequence of BBIs in a healthy child, it is one of the most tragic happenings that a physician may go through in a career [1].

Many previous US surveillance data have demonstrated a clear growth in morbidity and mortality in children due to BBI in the past two decades, enhanced public health and support efforts to highlight the danger of BBs for small children. The urgency to endoscopically eliminate esophageal batteries is now well be appreciated, however further consensus on management has been hard to develop [2,3]. From the clinical overview, there are two specific areas of management where there is considerable argument and/or ambiguity. First is the postremoval injury management in the children who swallowed a pointed objects and caused moderate/severe esophageal injury. Clinicians must first consider and try to minimize the spectrum of esophageal and para-esophageal complications connected with BBI in children and the specific management problems come across. The risk for late presence of aortoenteric fistula (AEF) days or weeks after BB removal further experiments the physician's decision making, specifically around patient appeal after battery removal [1].

The second point of contention in the management of BBI is the treatment of

asymptomatic individuals with batteries beyond the oesophagus (eg, intragastric, duodenal, and so forth). The Endoscopy Committee of the North American Society for Pediatric Gastroenterology, Hepatology, and Nutrition (NASPGHAN) recently advised considering endoscopic assessment and removal in certain cases of BBI if the battery lies beyond the oesophagus [3].

This advice contrasts prior National Battery Ingestion Hotline (NBIH) and National Capital Poison Center guidelines, which recommended only conservative initial care in asymptomatic children with postesophageal BB. The novelists evaluate their single-center experience with BBI in this paper with the primary goal of providing statistics that will assist better inform and support management choices [1]. A previous retrospective study was achieved to report the predisposing factors related with the complications of gastrointestinal (GI) tract foreign bodies (FBs) swallowing in children who went into surgical or endoscopic removal. This study was done in 161 children who had endoscopic or surgical removal of foreign body. The clinical recorded data were evaluated in two groups. In groups I and II, respectively, 135 patients with no complications and 26 patients with post-operative complications were analyzed. The risk factors were subjected to a relative risk analysis. In group I, the number of patients with an accurate history and radiopaque FBs was much greater. The most visible FBs in group II were metal, particularly sharp objects, and food plugs obstructing a sick oesophagus. In collection II, the majority of the FBs in both groups were entrapped in the oesophagus, the quantity of FBs distal to the oesophagus was much larger, and the period of lodgment was significantly longer. Esophageal laceration and bleeding, abrasion, caustic injury, severe esophageal stricture, complete esophageal obstruction, laryngeal edema, loss of weight, intestinal perforation, constipation, recurrent aspiration pneumonia and intestinal obstruction were recorded as complications. The relative risk was >1 for

duration of lodgment more than 24 h, for button batteries, sharp or pointed objects, nonopaque objects, morbid esophagus and for the objects located below the upper third of esophagus. Many factors of the ingested GI tract FB determine the significance and risk of the cases, such as; type, radiopacity, location and duration. A delayed diagnosis is the most significant influence increasing the risk of complications. The responsible physician of the case must maintain a high index of suspicion and a more extensive history; physical check and radiodiagnostic investigation should be obtained in assumed cases [4].

1.1 Objectives

This review article aimed to:

- Describe the pathophysiology of ingested foreign bodies.
- Outline the evaluation of a patient who has ingested a foreign body.
- Describe the treatment and management options available for ingested foreign bodies.
- Summarize interprofessional team strategies for improving care coordination and outcomes in patients who have ingested foreign bodies.

2. EPIDEMIOLOGY

The types of substances eaten differ depending on the patient's age. Coins accounted for 66 percent of upper GI foreign bodies discovered in patients younger than 10 years old, while food boluses accounted for 60 percent of upper GI foreign bodies detected in individuals older than 11 years old. In adult patients, food bolus impaction is frequently caused by an underlying anatomical defect, such as an esophageal web, ring, benign or malignant stricture, or eosinophilic esophagitis. In their sequences of 242 patients, 99 percent of ingested foreign materials became stuck in the upper GI tract; these foreign bodies were detected in the throat in 39 patients, the oesophagus in 181 patients, the stomach in 19 patients, and the small intestine in 3 patients [5].

3. PATHOPHYSIOLOGY

The majority (80%-90%) of foreign bodies and food impactions will pass spontaneously. Ten to twenty percent of gastrointestinal foreign bodies will require endoscopic intervention. Few patients who ingest foreign bodies require surgery [6,7]. Impaction, perforation, or obstruction most often

occurs at areas of acute angulations or physiologic narrowing. Potential sites for blocking include the cricopharyngeus muscle or upper sphincter, aortic arch, left main stem bronchus, gastroesophageal junction or lower sphincter, pylorus, duodenal sweep, ileocecal valve, and anus. Foreign bodies and food impactions in the esophagus have the highest incidence of complications with the complication rate directly proportional to the dwell time in the esophagus. Perforation is most common with sharp objects, and ranges from 15%-35% [6,8].

Materials retained in the upper GI tract generally fall into two groups, namely, a food bolus impaction and a true foreign body. Arrangements for foreign bodies, which define anatomic region and shape, are important for defining optimal therapy. Sharp-pointed objects, food bolus impaction, and button batteries may lead to upper GI tract perforation, obstruction or bleeding, thereby necessitating earlier intervention [5].

4. DIFFERENTIAL DIAGNOSIS

The differential for pediatric foreign body ingestion is broad, but the following entities should be considered (or ruled out) in patients presenting with such complaints:

- Esophagitis
- Pyloric stenosis
- Laryngitis
- Pharyngitis
- Globus sensation
- Esophageal rupture

5. LOCATION OF THE SWALLOWED FOREIGN BODY

5.1 Esophagus

Young children, unlike adults, unintentionally consume FBs. Esophageal FBs should be suspected in children who complain of a sore throat or difficulty swallowing saliva or meals for no apparent reason. If an esophageal FB is not passed spontaneously within 24 hours, it must be removed since it may cause an anatomical abnormality or esophageal perforation [9,10].

The Endoscopy Committee of the North American Society for Pediatric Gastroenterology, Hepatology, and Nutrition (NASPGHAN) recently amended its recommendations regarding the timing of endoscopic intervention. Regardless of the presence of symptoms, the presence of

esophageal button batteries necessitates prompt evacuation within 2 hours [11]. Coins, magnets, sharp FBs, or food impaction in the esophagus all order removal within 2 hours if the Children's secretions are uncontrollable. They may become separated within 24 hours in asymptomatic children. Long FBs lodged in the oesophagus must be removed within 24 hours, regardless of symptoms [12].

5.2 Stomach

If serial X-rays didn't show progressive movement of an ingested FB in asymptomatic children, it can be detected for 24 hours. Magnets reserved in the stomach in symptomatic children necessitate deletion within 2 hours. In asymptomatic children, they should be removed within 24 hours. In case of ingested coins in the stomach of symptomatic children should be removed within 24 hours. In asymptomatic children, these can be practical for 24 hours. Long or large FBs in the stomach require faster elimination for maximum within 24 hours [12].

The NASPGHAN Endoscopy Committee recommends foreign body elimination within 2 hours in a symptomatic children from the stomach irrespective of size [11]. For example; a button battery ≥ 20 mm located in the stomach of an asymptomatic children aged < 5 years should be removed fast within 24 to 48 hours.

5.3 Small Bowel

The majority of FBs in the small bowel are accepted spontaneously and without problems. As a result, doctors would console the children and/or caregivers and advise them to examine the children's stool for FB. If the FB is still there after a week, children should go to the hospital and get an X-ray to identify the precise position of the FB.

If children experience symptoms of intestine perforation or obstruction, such as vomiting, simple abdominal discomfort, fever, or intestinal bleeding, they should be firmly advised to go to the hospital as soon as possible. (12)

6. TYPES OF FOREIGN BODIES

6.1 Coins

Coins are one of the most commonly ingested FB in infants and children. Over 250,000 coin

intakes in children have been recorded in the United States [13]. There are many factors prompting the easy spontaneous passageway of a coin are its location in the esophagus, age of the child, and the size of the coin. Usually, the rate of extemporaneous passage of swallowed coins in children is approximately 30% [14]. Thus, children presenting with an ingested coin and experiencing no complications (a single coin wedged for < 24 hours, without any history of esophageal disease or surgery, and no respiratory symptoms) can be observed over 12–24 hours before presentation an invasive procedure (endoscopic or surgical elimination) [15]. Conners et al. suggested that coins stucked in the upper and mid esophagus require endoscopic removal, however they also reported that 60% of coins lodged in the lower esophagus have been experiential to pass spontaneously [16]. Coins that successfully pass through the esophagus are more likely to proceed and pass spontaneously [12]. Coins larger than 23.5 mm in diameter are more likely to be impacted, particularly in children under the age of five. Coins larger than 25 mm in diameter are unlikely to pass through the pylorus, especially in younger children, despite having successfully passed through the esophagus [17]. Children who have been witnessed or suspected of eating coins should have an X-ray to confirm the existence, size, and placement of the coin, and the inspection should be performed with care to distinguish the coin from a button battery, which exhibits the typical double halo indication. To reduce the possibility of problems, esophageal coins must be removed within 24 hours. Symptomatic youngsters who have difficulty swallowing saliva or breathing require emergent endoscopic removal. Following esophageal coin removal, a detailed endoscopic evaluation of the oesophagus mucosa is required to assess any evidence of serious harm.

In asymptomatic youngsters, ingested coins current in the stomach can be observed, and stool should be examined for coin passageway, and serial X-rays should be obtained every 1 or 2 weeks until coin passage is established. If the coin continues to remain in the stomach after 2–4 weeks, endoscopic removal can be explored. If the coin is found in the small bowel but the children are asymptomatic, a clinical remark should be made. However, in children who come with symptoms of intestinal obstruction or perforation, surgical removal should be considered [12].

6.2 Button Batteries

The incidence of button battery accidentally ingested has been increasing owing to the prevalent use of such batteries as power cradles in electronic devices [18]. Button batteries are just like coins in size and shape; thus, because these two FBs are the most often indistinguishable, a suspicious X-ray examination is needed to avoid a delay in diagnosis. Button batteries usually can cause severe damage secondary to innate hydrolysis and the action of hydroxide on the mucosa, caustic injury secondary to a high pH, and minor electrical burns inferior to lithium. Button batteries stuck in the oesophagus can cause burns in as little as 4 hours. Small button batteries (diameter 20 mm) do not usually create the major problems seen with bigger button batteries (diameter 20 mm) [19]. According to one study, all 7 children who consumed button batteries 15 mm in size were asymptomatic and had no difficulty, however all 5 children who ingested batteries larger than 15 mm in size had moderate (n=3) to severe (n=2) complications [20]. The author mentioned a 13-month-old infant who had eaten a 15-mm button battery 24 hours before the presentation. He arrived in the emergency hospital after vomiting and having poor oral intake for the previous day.

Unfortunately, no one knew he'd consumed the FB; however, an X-ray revealed a rotund metal FB with a halo indication in his upper oesophagus. An emergency endoscopic examination discovered a button battery that had caused an ulcer and esophageal mucosa degradation. Young children who receive awards with an uncertain/undetermined indication of ingested FBs require special care.

The NASPGHAN Endoscopy Committee recommends that esophageal button batteries should be removed within 2 hours [21]. However, the endoscopic removal of button batteries from the stomach remains a contentious problem. A comprehensive cohort study revealed that no earlier publications had indicated serious stomach wounds caused by button batteries [22]. As a result, the NASPGHAN Endoscopy Committee also suggests that asymptomatic children (aged less than 5 years) who present with a brief time of ingestion (less than 2 hours) of a small-sized battery (20 mm) be considered. Large batteries also (>20 mm) that remain after 48 hours must be removed fastly [12].

6.3 Magnets

Recently, the frequency of magnet swallowing in the infants and children has increased. If a single magnet is ingested, it should be passed immediately if it is not too huge. If multiple magnets or a single magnet with a metallic FB are ingested, the interaction between these ingested magnets or the magnet and the metallic FB and the mucosal surfaces of different body fragments can cause mucosal pressure necrosis, as well as intestinal obstruction, fistula, and/or perforation; therefore, surgical removal is desired in such cases [23,24].

If an X-ray reveals magnet ingestion, the physician must determine whether the ingested FBs are single or multiple magnets, or magnets with a metallic FB. Two or more magnets may occasionally be linked to each other and appear to be one piece, and misdiagnosis of multiple magnets as solitary magnet ingestion might result in delayed establishment of behaviour and substantial consequences. Given this risk, if numerous magnets or a single magnet with a metallic FB are placed within the oesophagus or stomach, even in asymptomatic youngsters, these FBs must be endoscopically examined.

If numerous magnets or a single magnet with a metallic FB are placed in locations other than the stomach, symptomatic children must contact a paediatric surgeon to plan surgery, while asymptomatic children can be closely watched using serial X-rays to track the course of the FBs. As adult toys, newer and smaller neodymium magnets that are at least 5 to 10 times stronger than traditional magnets have just been available, and they may fascinate each other with intense pressures [25]. On an X-ray, a neodymium magnet seems to be a ball bearing, and physicians should be cautious not to misdiagnose it as a metal ball.

6.4 Sharp or Pointed Foreign Bodies

Ingestion of sharp or pointed FBs in children is recognized to be associated with high morbidity and mortality, and delayed diagnosis and organization increases the risk of serious complications.

Sharp or piercing FBs, such as nails, safety pins, hairpins, pine needles, screws, thumbtacks, or dental prostheses, can result in serious complications such as trachea-fistula and/or abscess formation, esophageal ulceration and/or perforation, an aorto-esophageal fistula,

peritonitis, and even death [26,27]. Normally, intestinal FBs are known to induce perforation in 1% of patients; however, sharp or pointed FBs can cause perforation in 15%–35% of individuals. As a result, wherever possible, FBs should be removed from the oesophagus or stomach. Notably, in recent years, early detection and fast endoscopic removal have reduced the occurrence of adverse outcomes associated with the ingestion of sharp or pointed FBs [28]. For the ingestion of a sharp FB and an urgent X-ray examination, early diagnosis requires accurate information about the children's history or a high index of clinical suspicion. X-ray inspection cannot detect radiolucent FBs such as plastic, glass, fish bones, or wood. Thus, even if an X-ray does not reveal an FB in children with fictitious ingestion of sharp FBs, an immediate endoscopy is recommended.

A sharp FB current in the esophagus creates a medical state of emergency because of the high risk of perforation and migration and documents careful emergency removal even if the children have not been preserved on a nil per os status. Usually overtubes is used during endoscopic variceal band ligation when removing sharp FBs in adults, however their use is limited in children because of a great diameter. The use of an endoscopic cover to remove sharp FBs can prevent esophageal damage in children. If the FB's sharp end is found to be opposite the proximal site, it may be safe to push the FB into the stomach and rotate its sharp end to the distal site before removing it. Sharp or pointed FBs, long things (>4–5 cm in newborns and young children, >6–10 cm in older children), or huge and wide objects (>2 cm in diameter in infants and young children, >2.5 cm in diameter in older children) in the stomach should be removed endoscopically. In case of a sharp FB has migrated to the small bowel (distal to the ligament of Treitz), surgical elimination should be considered in symptomatic children. In asymptomatic patients, very close and careful clinical follow-up with serial X-rays obtained after admitting the patient are optional. The mean GI transit time for FBs in children is nearly 3.6 days [29]. Therefore, if the FB does not show the predictable passage after 4 days, a bowel perforation, intestinal obstruction or a congenital anomaly is suspected, and surgical exclusion of the FB should be careful [12].

6.5 Large or Long Foreign Bodies

The incorporation of large or long FBs is a particular concern. Long (>6 cm in length) or big

FBs are unlikely to pass over the duodenum and the ileocecal valve and must be removed within 24 hours. It has been reported that most of large or long FB swallowing cases were treated surgically or endoscopically as fast as possible [30].

Large or long items, lengthy substances (>4–5 cm in infants and young children, >6–10 cm in older children), or broad and wide substances (>2 cm in diameter in infants and young children, >2.5 cm in diameter in older children) in the stomach should be removed endoscopically [12]. It has been known that large, long or wide FBs can cause intestinal obstruction if left without removal more than 24 hours and can cause various complications.

6.6 Fish Bones

The most common food-related FB consumed by youngsters is fish bones. Both Korea and China, which have a high fish intake, have a higher frequency of fish bone incorporation than other countries [31].

Because the laryngopharynx is narrower and the tonsils are larger in children, fish bone impaction is more common in the palatine tonsils, tongue base, vallecula, and pyriform sinus. According to a Korean study, swallowed fish bones in youngsters were most typically found in the throat (57.7 percent) [32]. Fish bone impaction is, in fact, sporadic in the oesophagus below the throat. Fish bones jammed in the oesophagus, on the other hand, might produce mucosal ulcers or a topical inflammatory response, resulting in esophageal stenosis, perforation, a deep neck abscess, mediastinitis, a lung abscess, or uniform aortic fistulae. As a result, quick and precise identification and treatment are essential [12].

7. DIAGNOSIS AND EVALUATION

When a foreign body is suspected to have been ingested, the airway (particularly the oropharynx) and respiration should be checked as soon as possible. A foreign body that has become clogged within the oesophagus or has harmed it can induce chest pain or a foreign body sensation. When swallowing, symptoms may be more noticeable. Smaller children may drool, gag, vomit, or refuse to eat. Hematemesis and coughing may occur. Abdominal pain, vomiting, or bloody faeces may result from a foreign body stuck in the stomach or intestines. If the condition persists for an extended length of time, fever or

weight loss may emerge. More severe symptoms will be caused by a foreign body that has totally clogged the oesophagus.

The diagnosis is often seeming from the patient's case history. The patient may report a sudden onset of dysphagia while eating, may be accompanied by chest pain or odynophagia and an inability to handle secretions. When children are unable to provide a history, a sudden refusal to eat, drooling, or respiratory symptoms such as coughing or wheezing as a result of aspiration should alert the physician to the possibility of foreign body ingestion. A thorough physical examination should be performed to check for evidence of perforation, such as subcutaneous emphysema or peritoneal abnormalities. Drooling indicates total esophageal blockage. Plain radiography may reveal the foreign body; subcutaneous air, pneumomediastinum, or pleural effusion suggest perforation. Barium investigations have a limited yield as well; gastrographic imaging is not suggested in the obstructed oesophagus since it is hypertonic and might cause pulmonary edema if inhaled. CT scanning outperforms normal radiography in identifying foreign entities in 70-100 percent of patients [33,34].

When there is respiratory distress, airway compromise, or full obstruction is feared due to a patient's inability to handle internal secretions, an urgent endoscopy is indicated. Endoscopic diagnosis and treatment removal can be carried out concurrently [5].

8. MANAGEMENT

The majority of youngsters who swallow a foreign body do not require invasive treatment. Asymptomatic, previously healthy youngsters who have swallowed low-risk foreign bodies are usually fine. Patients and caregivers should be educated on the signs and symptoms of any problems that may arise. Medical treatment for foreign body ingestion is not advised. In the treatment of children with esophageal foreign bodies, emesis, muscle relaxants, and meat tenderizers are often useless and potentially hazardous. Laxatives are occasionally used to help items pass through the intestines, although this practise has not been demonstrated to be useful.

A clear history of a swallowed sharp foreign body or the possibility of an ingested sharp foreign body demands immediate radiographic

assessment. Radiographs have a 100 percent positive predictive value for metallic objects, but it is substantially lower for glass (43 percent), fish bones (26 percent), and wood, which is completely radiolucent [35,36]. If the x-ray is negative but there is still a high suspicion of a foreign body, it may be appropriate to proceed to endoscopic assessment. Otherwise, computed tomography scans, ultrasounds, magnetic resonance imaging, and upper GI barium swallow have been used to identify radiolucent foreign entities, but these may delay final therapy, particularly if contrast is employed [37-39]. Because of the significant potential of perforation and migration, a sharp object in the oesophagus is a medical emergency. Even if the patient has not fasted properly, it should be disconnected. If the patient shows signs of respiratory compromise, neck edoema, crepitus, or peritonitis, a surgical consult is required, and the patient should be transferred to an institution with appropriate expertise.

Once detected, the best management strategy is determined by the location and type of foreign material [40]. The success rate is then determined by the endoscopist's level of experience and the instrument used [41]. Magill forceps are especially useful for removing sharp foreign things such as fish bones from the oropharynx and upper oesophagus. For objects trapped at or above the cricopharyngeus, direct laryngoscopy can be used [42]. A flexible endoscope has the lowest complication rate for sharp foreign bodies below the cricopharyngeus [42]. It may be beneficial to simulate the foreign body prior to the procedure, and some endoscopists utilise a trial run to determine the optimum equipment for removal [43].

Retrieval forceps, a retrieval net, and a polypectomy snare are the best grabbing tools for sharp objects. However, the child's size will limit access to some devices, particularly if the patient weighs more than 5 kg. A 6-mm gastroscope has a 2-mm channel and will only fit small polypectomy retrieval nets (diameter 20 mm), polypectomy snares, or Dormia basket devices, as well as a few commercially available forceps. Sharp item removal from the upper GI tract with rat tooth forceps has been reported to have a 96 percent success rate. Polypectomy snares are useful for longer sharp objects like toothpicks and can be used to seal open safety pins in the stomach prior to extraction. If the object's sharp end is pointing cephalad, it may be safer to push the object into the stomach with rat

tooth forceps and rotate the sharp end caudally before removal [44].

8.1 Timing

Once foreign body ingestion is diagnosed, the physician must decide whether action is required, what level of urgency is appropriate, and what the best mode of intervention could be. The perceived risks of aspiration and/or perforation influence the timing of endoscopic intervention. Patients who have sharp items or disc batteries lodged in their oesophagus require immediate endoscopic intervention. Foreign bodies, such as food impactions, that cause blockage and the inability to regulate secretions also require immediate attention. Those who do not show signs of high-grade obstruction or acute distress can be treated less urgently because spontaneous passage may occur. However, no foreign item or food bolus impaction should be left in the oesophagus for more than 24 hours following presentation [5].

8.2 Sedation

The majority of adult patients tolerate conscious sedation. In most paediatric patients, general anaesthesia with endotracheal intubation provides complete airway protection. Furthermore, general anaesthesia with endotracheal intubation is preferable for the disobedient psychotic patient and those who have eaten many objects, extending the time required for extrication [5].

8.3 Prognosis

In general, the results and prognosis of paediatric foreign body ingestion are favourable, with most patients enduring the passage of ingested objects without intervention. Even when intervention is required, death and morbidity are low. Ingestion of high-risk items (button batteries, magnets) can result in problems and, in rare cases, death.

There have been reports of systemic responses related with zinc allergy. Foreign bodies in the oesophagus have been linked to mediastinitis, perforation, and pneumomediastinum. Because button batteries cause the most morbidity, they must be removed as soon as the diagnosis is made. Finally, operations to remove foreign bodies can result in difficulties due to the anaesthetic or the procedure itself.

9. CONCLUSION

For various scenarios, a number of endoscopic procedures and devices are recommended. For a professional endoscopist, flexible endoscopic therapy is a safe and dependable operation with a high success rate, little morbidity, and no mortality. EFBs are a fairly prevalent condition in juvenile patients, and underlying characteristics that predispose to EFB impaction are not uncommon. Long-retained EFBs are linked to an increased risk of problems. Rigid esophagoscopy was found to be a safe and effective approach for retrieving the majority of the EFBs.

CONSENT

It is not applicable.

ETHICAL APPROVAL

It is not applicable.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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