

PILL –INDUCED EROSIVE ESOPHAGITIS IN CHILDREN

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Abstract

Aims. Pill-induced esophagitis has been recognized in adults, but rarely in children. The aim of this article is to discuss endoscopic features, drugs implicated, prevention and treatment in pill-induced esophagitis in children.

Patients and methods. Over a period of 4 years, 26 patients presented at our clinic with drug-induced esophageal ulcerations. All patients were diagnosed by means of endoscopy and treated with proton-pump inhibitors and prokinetics. The mean age of the children was 10.76 years.

Results. The ulcers were frequently located at the mid-esophagus. Odynophagia, retrosternal pain and dysphagia were the most common presenting symptoms. All children took pills (non-steroidal anti-inflammatory drugs, antibiotics – Doxycycline and ferrous sulfate) with little water and at bed time. The mean elapse between the drug intake and endoscopy was 4.96 days. The symptoms resolved within a maximum of one week of antireflux therapy.

Conclusions. In pediatric cases treated by tablets or capsules, the possibility of medication-induced esophagitis should always be considered. The drug-induced esophagitis should be suspected in all patients presenting with chest pain and dysphagia. Physicians must warn the patients to take the pills and capsules with enough water and in the upright position.

Keywords: children, drug-induced esophagitis, endoscopic features, management

Introduction

Esophagitis is the most frequent esophageal disorder in children. Around 90 % of drug-induced esophagitis occur after use of non-steroidal anti-inflammatory drugs, antibiotics – doxycycline and ferrous sulfate [1,2,3,4,5]. Retrosternal pain, odynophagia and dysphagia are the most frequently reported symptoms.

The diagnosis is established by upper gastrointestinal endoscopy, which is also recognized as the method of choice. Double contrast studies detect also superficial ulcers and subtle mucosal changes. History alone may also be sufficient to establish a clinical diagnosis of esophagitis. Ulcers occur often at the level of the aortic arch and occasionally at the distal esophagus or very rarely at the proximal esophagus. Histopathological changes are non-specific and constitute necrosis and inflammatory exudate with lymphocytes and eosinophils predominance.

The clinical course is usually uneventful and severe complications are rare in children. Severe complications (including mortality) have been associated with iron and potassium. Usually, the disease is self-limiting. Symptoms frequently disappear within 7 days of symptomatic treatment and discontinuation of injurious drugs. It can be prevented by avoiding drug intake at bed time and ingestion of an adequate liquid amount.

The aim of this article is to increase the awareness of physicians and endoscopists on drug-induced esophageal ulcerations in children and to discuss endoscopic features, drugs implicated, prevention and treatment.

Patients and methods

In a retrospective analysis of 532 upper gastrointestinal (UGI) endoscopies performed by our endoscopists over a period of 4 years, 26 patients had drug-induced esophageal ulcerations. There were 16 girls (61.5%) and 10 (38.5%) boys with a mean age of 10.76 years. We mention that we have our patients' written consent regarding their inclusion in this study. Five patients were excluded

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from our study because the parents did not provide an informed consent.

The excluding 5 patients were not different from the studied population with regard to age, gender ratio and presence of symptoms. Odynophagia, retrosternal pain and dysphagia are the most frequently reported symptoms. Endoscopy was performed with a pediatric videoscope after a mean elapse of 4.96 days, utilizing 10% xylocaine spray for local anesthesia to all 26 patients. The number of ulcers and the distance from the incisors teeth were estimated also. After endoscopic diagnosis, children were asked to bring the drugs correlated with the development of the current symptoms. The patients were also asked about the timing of drug intake and the amount of concurrent fluid ingested. The patients were managed with proton-pump inhibitors and prokinetic agents such as metoclopramide or macrolide agents and when feasible, the injurious pills were withdrawn. All children were requested to give a feedback on their response after a week of treatment initiation.

Acid suppression with a proton pump inhibitor (PPI) is standard treatment for erosive esophagitis in adults and increasingly is becoming first-line therapy for children aged 1-17 years. Currently three PPIs are approved by the US FOOD and Drug Administration for the treatment of erosive esophagitis in children: esomeprazole (1-17 years), omeprazole (2-16 years) and lansoprazole (1-17 years).

Findings from direct comparative studies in adults show that esomeprazole more effectively heals erosive esophagitis in adults than omeprazole or lansoprazole. Patients were assigned randomly to esomeprazole (Nexium) 5 or 10 mg (children >8kg and <20 kg) or 10 or 20 mg (children >20 kg) once daily. For children aged <6 years or for those who had difficulty swallowing the capsules; capsule contents could be mixed with one tablespoon of apple sauce.

Results

Over a 4 years period 532 UGI-endoscopies were performed. The majority (466) were due to gastroesophageal reflux disease and peptic esophagitis. Drug-induced esophageal ulcers were found in 26 patients with different gender distribution (10 males and 16 females) (Figure 1). The age ranged between 8 and 15 (mean 10.76) years. All patients presented with odynophagia. Other symptoms are as shown in [Table 1]. Anti-steroidal anti-inflammatory drugs (Ibuprofen), antibiotics (Doxycycline) and ferrous sulfate were the only drugs incriminated in all patients (Figure 2). The drugs were prescribed for fever in 13 patients (Ibuprofen), acne in 7 children (Doxycycline) and anemia-iron deficiency (ferrous sulfate) in 6 patients. The elapse between drug ingestion and endoscopy was 4.96 days. The ulcers were found at 20 cm (mean distance) from the incisors teeth. In 3 patients ulcers occur at the distal esophagus and in one patient at the proximal esophagus. The surrounding mucosa appeared normal. The ulcers were variable in size, depth and number. The number ranged from one to six.

Repeat endoscopy four weeks after treatment revealed healed ulcers in the majority of children.

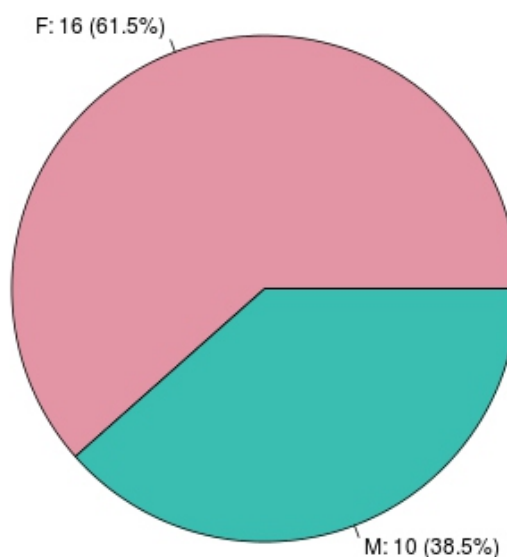


Figure 1. Gender Distribution

Table I. Clinical symptoms

SYMPTOM	Procentual values (%)
retrosternal pain	42
dysphagia	25
heartburn	12
vomiting	10
nausea	6
other	5

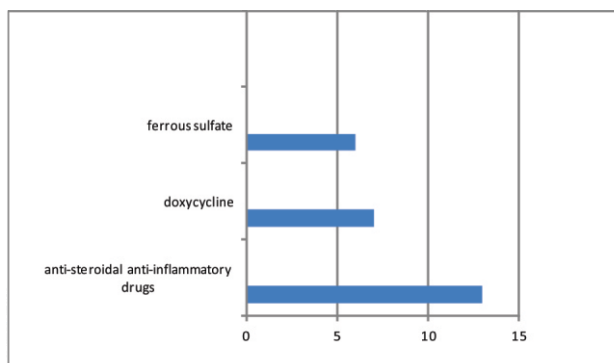


Figure 2. Drugs Distribution

All patients, except one, adhered to follow-up. Initial improvement occurred as early as 24 hours after treatment initiation in some children. After one week, most of the patients reported a complete resolution of symptoms. Eight patients developed complications (stenosis) and required a long time follow-up. One patient had no post treatment endoscopy (Figure 3).

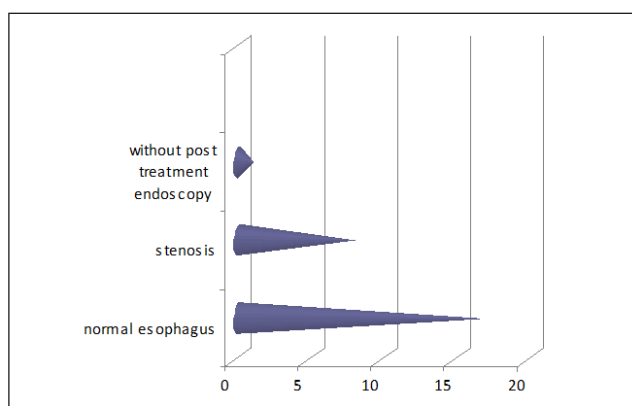


Figure 3. Evolution

Discussion

The prevalence of drug-induced esophageal ulcerations in this analysis was 4.88. Several drugs including antibiotics, anti-steroidal anti-inflammatory drugs, potassium chloride, quinidine, ascorbic acid and iron preparation may induce ulcerative esophagitis in children.

The drugs used by our patients were anti-steroidal anti-inflammatory drugs, doxycycline and ferrous sulfate. The risk factor was drug intake at bedtime with little fluid in all children. During recumbent position and sleep, salivation and swallowing are reduced and esophageal transit time is prolonged, which causes drug retention in the esophagus. Pre-existing esophageal disease and external esophageal compression, due to left atrial enlargement, precipitate also drug-induced esophageal ulceration, but none of our children had a history of a pre-existing esophageal or cardiac disorder [6].

Drug retention and the acidic property of a drug such as doxycycline and ferrous sulfate, may explain its injurious esophageal mucosal effect [7,8]. Esophagitis associated with anti-steroidal anti-inflammatory drugs is linked with a mucosa altered protective function due to decreased prostaglandine synthesis [9].

The ulcers were located mainly at the midesophagus. This is in accordance with other reports where the mid-esophagus was found to be the commonest site [3,10]. In 3 patients ulcers occurred at the distal esophagus and in one patient at the proximal esophagus, an uncommon position. The ulcers number and size were variable. They were small and/or large, single or multiple, mostly facing each other with apparently normal surrounding mucosa. Extensive ulcers involving a large portion or the entire esophagus reported in adults are atypical for drug-induced esophageal injury in children. We have not encountered such a severe and extensive esophageal injury.

The main presenting symptoms of our patients were odynophagia, retrosternal pain and dysphagia. This is in agreement with other reports, where retrosternal pain, odynophagia and dysphagia are the most frequently reported symptoms also [5,11]. Heartburn ranged as the fourth

commonest symptom.

Endoscopy is the method of choice for confirming the clinical diagnosis. Double contrast barium swallow is also accurate and may detect even subtle mucosal changes, but a single contrast study may give wrong negative results in children. Complications (stenosis) were encountered in this analysis in 8 patients. Complications have been reported in association with anti-steroidal anti-inflammatory drugs. This is also in agreement with other reports. Drug-induced esophagitis is usually a self-limiting disease and symptoms resolve within 7 to 10 days.

We agree with other authors, who have considered injurious drug withdrawal as the main step of management. However, we feel anti-steroidal anti-inflammatory drugs, doxycycline or ferrous sulfate therapy can be continued when required with emphasis on patients and their parents education in regard of the timing of medication and the amount of fluid required. Many patients became asymptomatic within the first week of treatment with proton-pump inhibitors and prokinetics. Only eight children required a long time follow-up.

The benefit of commonly used medications including antacids, sucralfate, H₂-receptors antagonists and proton-pump inhibitors for treatment of drug-induced esophageal injuries is real. The symptoms improved soon after initiation of treatment and ulcer healing was confirmed by endoscopy.

Conclusions

In the current study, anti-steroidal anti-inflammatory drugs, doxycycline and ferrous sulfate were responsible for all drug-induced esophageal ulcerations. The presence of odynophagia and retrosternal pain should raise the suspicion and necessitate exploration of drugs history and endoscopy to confirm the diagnosis. Withdrawal of medicine is the main step of management when feasible. Children and their parents' education and the use of alternative drugs in patients at risk are important to prevent drug-induced esophageal ulcerations. Proton-pump inhibitors and prokinetics are also an important step of management in children.

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