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

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).

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.
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, H 2 -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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