



Original Article

Drug-Induced Esophagitis in a Tertiary Care Hospital

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Abstract

Drug induced esophagitis, also known as pill-induced esophagitis or drug-induced esophageal injury, is uncommonly encountered in clinical practice. This observational study was jointly carried out by the Department of Medicine and Department of Gastroenterology, Rajshahi Medical College, from January 2005 to December 2009. Total number of patients included was 32. Patients who presented with history of odynophagia and chest pain after ingesting some medications and having endoscopic evidence of esophagitis were included in this study. Out of 32 patients 17 were female and 15 were male (F: M=1.1:1). Mean age of the patients were 36.7 ± 8.5 years. Doxycycline was the drug most commonly associated with esophagitis, 25 cases (78.1%) had doxycycline induced esophagitis. Other drugs were tetracycline in 3 cases (9.4%), alendronate in 1 case (3.1%), ciprofloxacin in 1 case (3.1%), paracetamol in 1 case (3.1%), and naproxen in 1 case (3.1%), Increased awareness among the physicians and patient education can prevent this distressing clinical condition.

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Introduction

Drug induced esophagitis, also known as pill-induced esophagitis or drug-induced esophageal injury, is uncommonly encountered in clinical practice. Documentation of esophageal mucosal injury induced by the local caustic effect of medication was first described in a patient who ingested potassium chloride tablets.¹ It is likely that drug induced esophageal injury was also prevalent prior to that time, but were not diagnosed because of unawareness about this condition and the relative lack of flexible fiberoptic endoscopy. Since the initial report, the frequency of drug-induced esophageal number has continued to grow worldwide. The reported incidence of induced esophagitis is approximate incidence of 4/100 000 is probably underestimated. The actual incidence is apparently much higher because of increase in drugs prescription and failure of reporting.^{2,3} History has

been considered sufficient for assuming a clinical diagnosis.^{4,5} Retrosternal pain and sudden odynophagia with or without dysphagia are suspicious of the diagnosis.² History of medication, time of drug intake and amount of concurrent fluid ingested are important.^{6,7} Upper gastrointestinal endoscopy is almost always abnormal and it has been considered as the method of choice to confirm drug induced esophagitis.²

In Bangladesh, because of poor regulations, almost everyone can buy almost any drug from drugstore without prescription. Because of low cost, and availability in hospital dispensary, doxycycline, and tetracycline are widely prescribed in the OPD of government hospitals of Bangladesh. Large number of prescriptions, over-the-counter availability and inadequate counseling by the physicians, are probably responsible for growing number of drug-induced esophagitis in this country.

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Aims and objectives

The aim of this article is to increase the awareness of the physicians regarding this fairly common but preventable disease, drugs commonly responsible for it and its prevention and treatment.

Material and Methods

This observational study was jointly carried out by the Department of Medicine and Department of Gastroenterology, Rajshahi Medical College from January 2005 to December 2009. Total number of patients included was 32. Informed written consent was taken from the patients prior to enrollment. For all study subjects preformed questionnaire was used to collect data. Patients who presented with history of odynophagia and chest pain after ingesting some medications and having endoscopic evidence of esophagitis were included in this study. Patients with long history of heartburn, history of corrosive ingestion and patients who decline endoscopy were excluded from the study. Collected data were processed and analyzed with SPSS software version 12.0.

Results

Out of 32 patients 17 were female and 15 were male (F: M=1.1:1). Mean age of the patients were 36.7±8.5 years.

Table 1: Drugs associated with esophagitis (n=32)

Drugs	Number of cases	Percentage
Doxycycline	25	78.1
Tetracycline	3	9.4
Alendronate	1	3.1
Ciprofloxacin	1	3.1
Paracetamol	1	3.1
Naproxen	1	3.1

Table 2: Presenting symptoms (n=32)

Symptom	Number of cases	Percentage
Odynophagia	32	100
Retrosternal pain	23	71.9
Dysphagia	14	43.8

31 patients (96.9%) has taken the offending drug at bedtime with little water, and woke up in the next morning with odynophagia. one patient (3.1%) took alendronate in the morning but failed to follow the standard precautions. The mean elapse between drug intake and endoscopy was

7.53 ± 2.6 days. Upper GI endoscopy demonstrated that, in 26 cases (81.2%), the site of ulceration is distal esophagus, in remaining 6 cases (18.8%) the ulcers were in mid-esophagus. 25 patients (78.1%) had multiple ulcers and the remaining 7 patients (21.9%) had solitary ulcer. All of the patients were treated symptomatically. Mean time of symptomatic improvement was 7.23 ±2.1 days.

Discussion

Drug-induced esophagitis may occur at any age and with a variety of commonly used medications.⁸ The incidence of drug-induced esophagitis has been estimated as approximately four cases per 100,000 per year.⁹ Commonly implicated medications include tetracycline's (especially doxycycline), sustained release potassium preparations, non-steroidal anti-inflammatory drugs (NSAIDs) (especially Aspirin), quinidine, bisphosphonates and emepronium bromide.¹⁰

The mechanism of injury is believed to be due to prolonged contact of the caustic contents of the medication with the esophageal mucosa. This theory is supported by animal studies in which lesions identical to those found in patients were induced by direct mucosal placement of the same medications.^{11,12}

Clinically, this hypothesis is supported by the typical esophageal lesion showing a small punched out ulcer in a limited area that was conceivably in contact with a high concentration of medication released from a dissolving drug. In addition, the site of injury is frequently found in areas in which the esophageal lumen is compromised by the aortic arch, the esophago-gastric junction, or an enlarged left atrium. Thus, medication-induced injury requires that the pill or capsule remain in the esophagus for a prolonged interval, and that its contents be inherently caustic to the esophageal mucosa. Some degree of esophageal retention of pills or capsules occurs in normal individuals. However, the following situations enhance pill retention, thereby increasing the likelihood of esophageal injury: lack of an adequate liquid bolus and a long period in the recumbent position is

believed to play a major role in pill retention. Ingestion of a drug immediately prior to sleep favors prolonged retention since salivation and swallowing frequency are markedly reduced during sleep.^{13,14} The proposed mechanisms of caustic injury induced by various drugs include the following: A local acid burn may be caused by medications such as doxycycline, tetracycline, ascorbic acid, ferrous sulfate, and emepronium. Each of these compounds has a pH less than 3 when dissolved in distilled water or saliva.¹⁵ However, other equally caustic medications such as clindamycin, potassium chloride, and quinidine do not alter pH. Local hyper-osmolality from high concentrations of dissolving medication may be capable of tissue destruction and vascular injury, a mechanism suggested for potassium-induced lesions.¹⁶

The typical patient with drug-induced esophagitis does not have a history of prior esophageal disease. Patients will often present with the sudden onset of odynophagia and retrosternal pain; the pain may be so severe that swallowing saliva is difficult. Patients often relate (after careful questioning) the onset of symptoms to the swallowing of a drug without water, commonly at bedtime. Drug-induced esophagitis is often suspected when typical symptoms appear abruptly after improper ingestion of a drug known to cause esophageal injury. In these cases, a clinical diagnosis may be made without the requirement for confirmatory endoscopy or barium radiography. However, diagnostic confirmation becomes more important in patients with particularly severe or atypical symptoms, or if an alternate diagnosis is likely. Flexible upper endoscopy is the most sensitive procedure; findings are abnormal in virtually 100 percent of cases.¹⁷ Endoscopy is also helpful to rule out alternate diagnoses such as reflux esophagitis, infectious esophagitis, or malignancy. The typical endoscopic appearance of drug-induced esophageal injury is a discrete ulcer with relatively normal surrounding mucosa.¹⁷ The ulcers may range in size from 1 or 2 mm to several centimeters long. They may be single or multiple and may be surrounded by mild local

inflammatory changes. Although the typical ulcer involves only the mucosa, deeper degrees of penetration can occur and localized perforation has been described.^{18,19} The lesion rarely may be characterized by a profuse exudate with nodularity suggestive of a polypoid neoplasm; this finding is particularly true with quinidine-induced injury.²⁰ Esophageal stricture is also relatively rare; when it occurs, anti-inflammatory drugs are typical causes.²¹

The true incidence of drug-induced esophagitis is probably still higher because of under-reporting, missed diagnoses, and subclinical episodes. Experts agree that there is an increase in incidence of drug-induced esophagitis in the developed world because of the increasing age of the population and higher rates of prescription of drugs.²² Most cases of medication-induced esophageal injury heal without intervention within a few days.²³

The cornerstone of treatment is prompt discontinuation of the offending drug. If it is necessary to continue the medication, a parenteral or liquid formulation could be substituted, keeping in mind that liquid formulations of some compounds are also noxious to the esophageal mucosa.⁸ Ideally, medications should never be given at bedtime or prior to lying down, as these behaviors cause significant changes in esophageal motility. Patients should be encouraged to take their medications one pill at a time and with at least 75 to 100 mL of liquid.⁸ Patients should be warned against taking medication within 1 hour of bedtime. The currently available treatments for the relief of pain associated with drug-induced esophagitis are sucralfate, H₂ receptor antagonists, lignocaine viscous, and proton pump inhibitors. They are ineffective and not standardized and approved by FDA.⁸ Sucralfate binds to ulcerations in the esophagus caused by the drug. A proton-pump inhibitor (PPI) or H₂ receptor antagonist is commonly used with the idea that reduction of acidity might help symptomatically. Lignocaine viscous which has an anesthetic effect but may not stay over the ulcer and it is difficult to target the ulcer when administered orally, hence complete relief is not obtained. Most patients can be

managed in outpatient basis but in some the retrosternal pain and dysphagia can be severe enough requiring hospitalization and further treatment.

Conclusion

Drug-induced esophagitis is being increasingly recognized in clinical practice in Bangladesh. Physicians must be aware about the drugs which may cause esophagitis and should counsel the patients adequately about the preventive measures while prescribing these drugs.

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