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Incidence of Cardiac Drugs to Cause Pinpoint Odynophagia as a Differentiating Sign of Pills Induced Esophagitis in Patients Presenting with Angina

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Abstract

Objective: Our aim of present study is to evaluate incidence of pinpoint odynophagia in clinical profile of drug induced oesophagitis (DIO) and its correlation with endoscopic findings particularly kissing ulcer. *Materials and Methods:* We have studied demographic features, clinical profile and endoscopic findings of cardiac DIO patients from August 2014 to January 2017 at various hospitals of Ahmedabad, India. Overall patients having history of retrosternal chest pain and odynophagia of less than 10 days' duration preceded by pill ingestion were clinically diagnosed as DIO and were subjected for upper GI endoscopy. All patients were investigated to rule out other causes of chest pain. Patients of infective and corrosive oesophagitis, oesophageal malignancy, chronic liver or kidney diseases and GERD of more than two weeks were excluded from the study. *Results:* We have studied total 248 patients of DIO and out of these 171 were females. Retrosternal chest pain and odynophagia were present in all patients and pinpoint odynophagia was present in 154 (62.10%) patients, out of them DIO due to cardiac drugs were 22.05%. Upper GI endoscopy showed kissing ulcers at middle third of oesophagus in 74.19% (p value =0.03). History of taking evening pill dose 5-10 minute before going to bed and habit of using less than 100 ml water to swallow pill were present in significant number of patients. *Conclusion:* Twenty percent of the patients presented with DIO had cardiac drugs responsible for reterosternal chest pain. Pin pointing localised odynophagia is very specific symptom of cardiac DIO and correlate well with kissing ulcer of oesophagus by upper GI endoscopy. Habit of taking evening pill just before retiring to bed and use of less than 100ml water to swallow pill were significant risk factors.

Keywords: Cardiac Drug Induced Oesophagitis (DIO); Pin-Point Odynophagia; Upper GI Endoscopy; Kissing Ulcer.

Introduction

Many drugs like some cardiac drugs, antibiotics, nonsteroidal anti-inflammatory drugs (NSAIDs), oral iron preparations, Bisphosphonates, potassium chloride, acetyl salicylic acid, quinidine, alprenolol can cause drug induced oesophagitis (DIO) by various mechanisms [1,2].

Medications can induce oesophageal abnormalities via both local and systemic effects like local caustic effect of pill chemical, prostaglandin E2 blockage by COX2 inhibition and mucosal injury or by change in oesophageal motility. Drug induced oesophagitis is a least discussed and under diagnosed clinical entity at present [3]. However lack of awareness of drug induced oesophagitis can lead to persistent exposure of offending drug and may

lead to complications like perforations, bleeding and later on structure[4,6]. Patients of DIO who are not included in differential diagnosis of chest pain may be subjected for unnecessary diagnostic evaluation of chest pain[5]. The possibility of DIO should be suspected in patients who complain of retrosternal chest pain, odynophagia or dysphagia [2]. Drug induced oesophagitis is a clinical diagnosis and upper GI endoscopy is a gold standard diagnostic procedure for confirmation of this diagnosis. Upper GI endoscopy is also useful to find complications and to rule out other oesophageal diseases like malignancy, eosinophilicoesophagitis and infective etiology.

Oesophageal ulcer biopsy shows various nonspecific inflammatory changes in DIO, but is useful to rule out malignancy. Patient factors like using less water to swallow pill, taking pill in supine position and just before going to bed are important risk factors for DIO. Middle third of oesophagus is compressed by aortic arch, left atrial enlargement and are important contributors in DIO [5]. We have observed pinpoint odynophagia in many patients of DIO and this symptom may be due to deep kissing ulcers (ulcer facing each other) caused by the causative pill including cardiac pill. None of the previous studies or literature has mentioned pinpoint odynophagia and its relation with DIO especially drugs related to cardiac diseases. For this reason, one of our aim for present study was to evaluate this symptom and to study its clinical profile and endoscopic features in DIO, including the one having cardiac drug origin. Other objectives of present study were to analyse clinical profile, riskfactors, clinical outcomes and endoscopic findings of DIO.

Materials and Methods

This cross-sectional prospective study of cardiac drug induced oesophagitis was done from August 2014 to January 2017 at multi-speciality Hospital at Ahmedabad after taking consent of each patient and necessary permission from the respective institute.

Inclusion Criteria

Definite history of taking pill and followed by acute oesophageal symptoms like retrosternal chestpain, odynophagia, dysphagia or nausea of less than 10 days duration.

Exclusion Criteria

Oesophageal or other malignancy, Infective oesophagitis, corrosive oesophagitis, chronic liver or kidney disease, oesophageal reflux symptoms of more than two weeks.

After clinical diagnosis of DIO, other causes of chest pain where excluded by relevant investigations like x-ray chest, electrocardiogram etc. All patients were subjected for echocardiography for chest pain evaluation and to rule out left atrial enlargement and unfolding of aorta. All patients were subjected for upper GI endoscopy and oesophageal lesion biopsy was taken. Rapid urease test was done to rule out *H.pylori* infection.Statistical analysis of data was done with Epi info software.

Results

We have studied total 248 patients of cardiac DIO and out of that 171 were female and 77 were male. Retrosternal chest pain, chest pain radiating to interscapular region, pinpoint odynophagia, odynophagia non localised and dysphagia were present in 62.1%, 37.9%, 62.1%, 37.9% and 31.45% respectively (Table 1).

Indoor treatment was required in 25.4% patients Diagnosis other than DIO by other clinicians were present in 37.5% cases. History of taking pill in evening 5-10 minute before going to bed was present in 35.88 % and habit of swallowing pill with less than 100ml water was present in 38.31%cases (Table 2).

History of taking azithromycin, doxycycline, aspirin, NSAIDs, clopidogrel and other cardiac drugs, unidentified origin were 12.5%, 18.55%, 6.05%,6.45%, 16% and 40.32% respectively (Table 3) and cardiac drugs were 22.05% (aspirin – 6.05%, clopidogrel and other cardiac drugs – 16%).

Upper GI endoscopy showing kissing ulcer at middle third of oesophagus with surrounding small discrete ulcer of 2-6 mm size were present in 74.19%, multiple small discrete ulcers of 2-10 mm size in 17.74% and erosions in 8.06% were present at lower third of oesophagus (Table 4).

All the patients were treated with proton pump inhibitor and sucralfate along with symptomatic treatment after discontinuing causative drug. 78 (31.4%) patients were followed up with endoscopy, where they revealed normal findings or well healed scar in the oesophagus.

The remaining 170 (68.55%) patients had no symptoms during follow up and did not undergo endoscopy or were lost from follow up. Endoscopic finding of kissing ulcer is shown in Figure 1.

Table 1: Demographic Features and clinical symptoms of Patients diagnosed with drug induced esophagitis *n* (%)

Characteristics		
Age (year)	Mean ± SD	33.58 ± 11.09
Sex	Male/ Female	77/171
Symptoms	Retrosternal Chest Pain non-radiating	154 (62.1%)
	Retrosternal chest pain radiating to interscapular region	94 (37.9%)
	Odynophagia pin point	154 (62.1%)
	Odynophagia diffuse	94 (37.9%)
	Dysphagia	78 (31.45%)
	Nausea	50 (20%)

Table 2: Endoscopic comparison of various clinical features

Clinical feature: n (%)	**Kissing Ulcer on Middle 3rd of Esophagus: n (%)**	**Multiple small erosions and ulcers at lower 3rd of Esophagus: n (%)**
Pinpoint odynophagia: 154 (62.10)	122 (49.19)	32 (12.90)
Odynophagia non-localized: 94 (37.90)	62 (25.00)	32 (12.90)
Indoor treatment required: 63 (24.50)	63 (24.50)	Nil
Habit of taking pill with less than 100ml of water:95 (38.31)	74 (29.84)	21 (08.47)
Evening dose pill just before going to bed:89 (35.88)	70 (28.22)	19 (07.66)

Table 3: Drug identified as a Possible Causative Agent n (%)

Drug	**N (%)**
Doxycycline	46 (18.55)
Azithromycin	31 (12.50)
NSAIDs	16 (06.45)
Unidentified pill	100 (40.32)
Cardiac Drugs	
Aspirin	15 (06.05)
Clopidogrel and other cardiac drugs	40 (16)

Table 4: Endoscopic features of patients diagnosed with drug induced oesophagitis

Feature		**N (%)**
Location	Middle third oesophagus	184 (74.19)
	Distal third oesophagus	64 (25.81)
Endoscopic Finding		
	Kissing Ulcer	184 (74.81)
	Erosions	20 (08.06)
	Discrete Ulcers	44 (17.74)
	Drug deposits at ulcer base	17(06.85)

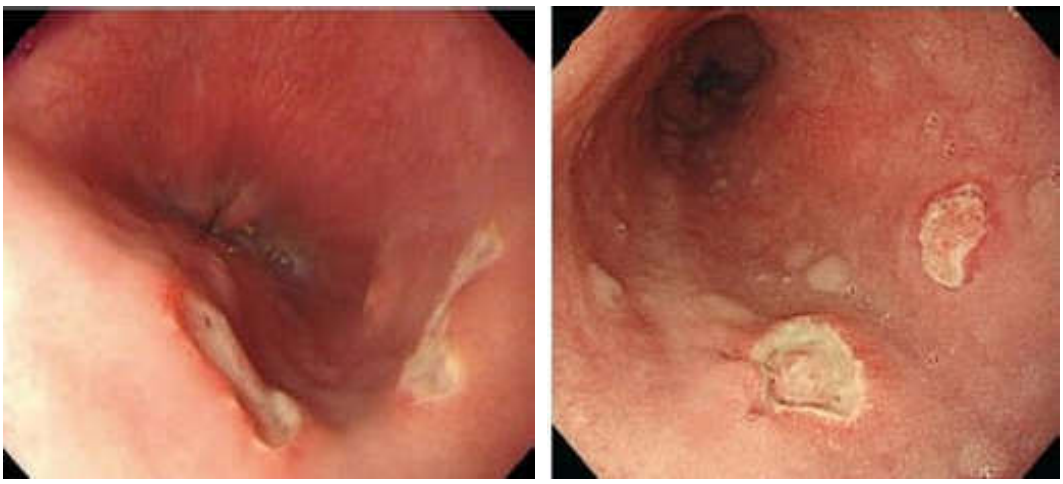

Fig. 1: Endoscopic Finding: Kissing Ulcer of middle 3rd of esophagus

Discussion

Our study showed the incidence of DIO due to cardiac drugs was 20.05% and overall DIO was more common in females (68.95%). This is consistent with previous study of AbidSet al [7]. There are reports that DIO is predominantly found among elderly patients as they are more likely to spend time in the recumbent position, consume more medication, have oesophageal dysmotility or left atrial enlargement causing mid oesophagus compression [5]. However, in our study cardiac DIO was more common in young patients (mean age 33.58±11.09) and reason may be higher use of antibiotics by young people or patient related factors like evening pill dose at bedtime or taking pill with lesser amount of water. Evening pill dose 5 to 10 minutes before retiring to bed may keep pill for a long time in the oesophagus because of supine position [8]. In our study this was a significant risk factor for DIO. Habit of pill swallowing with lesser amount of water is also a risk factor for cardiac DIO (p value 0.02). Pill may not be transported to stomach and trapped to oesophagus if lesser amount of water is used [9]. Zografos et al [3] showed that the main symptoms in cardiac DIO were chest pain (60%), odynophagia (50%)and dysphagia (40%). In contrast to Our study showed all patients had chest pain and odynophagia and dysphagia in 31.45% of patients. Pinpoint localised odynophagia means patient can locate exact site of pain was a new symptom of cardiac DIO in our study. No previous study has evaluated pinpoint odynophagia as a symptom of cardiac DIO. Our study showed pinpoint odynophagia in 62.1% of total patients and it was correlated with kissing ulcer oesophageal location by endoscopy. Many studies showed that lesions of DIO were in middle third of oesophagus. This part of oesophagus is prone for compression by aortic arch and enlarged left atrium [5,10,11]. In our study 74.19 patients had lesions in middle third of oesophagus and it was matching with previous reports. Significant numbers of patients were having severe symptoms and they required indoor treatment. So, it is important to diagnose DIO early to prevent complications [4-6]. Doxycycline was most common causative drug but many unidentified drugs also caused DIO. These unknown drugs were either dispensed by family doctor or purchased from chemist over the counter. Upper GI endoscopy is a gold standard procedure for confirmation of clinical diagnosis of DIO, its complications and to rule out other oesophagogastric pathologies. Endoscopic findings of cardiac DIO were kissing ulcer (ulcer facing each other), erosions or multiple ulcers of various sizes. If drug deposit or pill fragment is present at oesophageal ulcer site, clear diagnosis of DIO can be established. In our study 6.85% of total patients were having drug deposit at ulcer site and it was matching with study of SU Hwankin et al [5]. They showed 8.5% patients were having drug deposit at oesophageal ulcer site.Cardiac DIO should be considered in all patients of chest pain and odynophagia and they should be subjected for endoscopy for confirmation of the diagnosis.

Conclusion

In conclusion, 22.05% of the patients with DIO had cardiac drugs responsible for reterosternal chest pain. Pinpoint localised odynophagia was a specific symptom of DIO, identified in our present study. Kissing ulcer by endoscopic wasthe commonest and specific findingand it wascorrelated with pinpoint odynophagia as kissing ulcers were present in all of them.

Conflict of Interests

The authors confirm that this article content has no conflict of interest.

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