Medical Journal of The
Islamic Republic of Iran

Volume 2, Number 1
Bahar 1367
Shaaban 1408
Spring 1988

DOXYCYCLINE-INDUCED ESOPHAGEAL ULCER

R. MALEKZADEH

From the Department of Medicine, Shiraz University of Medical Sciences, Shiraz, Islamic Republic of Iran

ABSTRACT

During a period of 4 years (1983-1986), we have seen 18 patients with esophageal ulcer following the intake of doxycycline capsules at the University Hospitals of Shiraz Medical School. During the same period only one other patient with a drug-induced esophageal ulcer was seen and this was found to be due to a mefenemic acid capsule.

Diagnosis was made by esophagoscopy and after two weeks, follow-up endoscopies revealed complete healing of the ulcers. After one year, the follow-up observations of ten patients revealed no stricture or obstruction. We conclude that doxycycline capsule is the single most common cause of drug-induced esophageal ulcers and although a self-limited complication, in already ill patients, it produces significant morbidity which could be prevented by simple measures.

MJIRI, Vol.2, No.1,33-35, 1988

INTRODUCTION

Caustic esophageal injury, either accidental or due to suicidal attempt, is a well recognized entity. During the last two decades, several reports have clearly shown the hazards of esophageal injury from normal doses of certain therapeutic agents.[14-16] During a four year period (1983-1986) in Shiraz, 18 patients who had ingested doxycycline, and one patient who had taken a mefenemic acid capsule were examined and found to have developed esophageal ulcerations.

In this paper, we will describe the clinical and pathological features of these patients as well as the measures recommended to avoid this potentially hazardous complication of an otherwise safe and effective drug.

PATIENTS AND METHODS

During a period of 4 years (1983-1986), 18 patients who presented with dysphagia and odynophagia 4-6 hours following the last dose of doxycycline capsules were seen in the outpatient department of the University Hospitals of Shiraz Medical School. During the same period, one other case of drug-induced esophagitis was seen which occurred 3 hours after the ingestion of mefenemic acid capsules.

Upper gastrointestinal fiberoptic endoscopies were performed in the first eight patients and in three of these patients, endoscopic biopsies were also obtained. In the remaining ten patients, the strong temporal association between the oral ingestion of doxycycline capsules and the onset of dysphagia as well as the similarity of their clinical course to the previous patients, strongly suggested that these cases also represented doxycycline-induced esophageal ulceration. Follow-up endoscopies were performed in five patients 2 weeks later. A complete history including a meticulous drug history, a thorough physical examination and routine blood tests were obtained in all patients. Periodic follow-up examinations were done in 10 patients for an average period of one year. Patients were treated with liquid and soft diets along with liquid antacids for pain relief.

RESULTS

There were 7 male and 11 female patients, 12 patients were aged 19-30 years, while 6 patients were between 30 and 40 years. Doxycycline capsules had been

[Downloaded from mjiri.iums.ac.ir on 2025-04-08]

prescribed to treat acne, pelvic infections, or sinusitis. All patients became symptomatic after taking the capsules at bed time without adequate water.

All patients developed severe substernal pain, occasionally radiating to the back, which was aggravated by eating food or drinking. Pain was severe during the first three days, thereafter decreasing in intensity until the complete relief of pain within the following 10-14 days. Esophagoscopy revealed either a single large circular or multiple small esophageal ulcers involving the lower one third of the esophagus. In three patients there was evidence of a hiatal hernia with mild esophagitis. Endoscopic biopsies revealed acute inflammation and ulceration with no evidence of fungal infections. In five patients, follow-up fiberoptic esophagoscopies were completely normal with no evidence of stricture or narrowing. All patients who came for follow-up examinations after an average period of one year, were asymptomatic.

One of the patients also had rheumatic heart disease causing mitral stenosis and left atrial enlargement, but neither this patient nor any of our other patients had taken any other ulcerogenic drugs, e.g. potassium chloride. None of the patients showed any other significant clinical or paraclinical finding during this study. None of the patients had been informed by their prescribing physicians that they should take adequate water with the capsules.

DISCUSSION

There is a misconception among clinicians regarding the passage of orally administered medications through the esophagus, and it is assumed that ingested drugs reach the stomach rapidly and without delay. Ewans and Roberts[8] in 1976 showed that barium sulphate tablets, identical in size and shape to those of aspirin, can remain in the esophagus for up to ninety minutes after ingestion. Both they and others [4-7] have clearly shown that retention can even occur in those without symptoms or signs of esophageal disease. The incidence of retention is significantly increased in those with esophageal abnormalities.[6-15] In 1982, Hey, et al showed that to ensure a rapid transit of large tablets through the esophagus when the patient is either standing or recumbent, it is essential to take the medication with 100 ml of water, but that the quantity of water taken has no effect on the passage of capsules. These authors recommend liquid medications for patients who are bedridden or have difficulty in swallowing instead of tablets or capsules.

The pathogenesis of drug-induced esophageal ulcer is that the capsule or tablet remains in the esophagus for an hour or more because it may be held up by an anatomical (e.g. aortic arch) or pathological narrowing, [15] (e.g. enlarged left atrium) or the patient does not totally swallow the tablet or capsule and immediately goes to bed.[4-7] When swallowed with too little fluid, the tablet or capsule's hygroscopicity can cause the drug to stick to the esophageal mucosa. This contact with the mucosa results in its rapid disintegration, creating a high concentration of the ulcerogenic agent which in the case of a doxycycline capsule, has a pH of less than 3, and produces esophagitis and esophageal ulcer.[12,18,20]

This study clearly shows that doxycycline is the single most common cause of drug-induced esophageal ulcer in our area as has been shown worldwide,[13] but other drugs can also potentially produce esophagitis or an esophageal ulcer in usual therapeutic doses, even in patients with a normal esophagus. Although there have been reports of esophageal perforation, mediastinitis and even death with some drugs, all our patients recovered inspite of considerable pain.[2,5,16]

To avoid morbidity and patient suffering due to this complication of an otherwise safe and effective drug, particular care must be exercised by the prescribing physician, especially in patients with a preexisting esophageal obstruction. In general, the tablets and capsules should be taken with at least 100-150 ml of water and when possible, patients should remain standing for 1-2 minutes after taking capsules or tablets. Liquid forms of medication are preferred for bedridden patients. Drug manufacturers should try to produce a safer formulation for ulcerogenic drugs (e.g. doxycycline) and by directions written on the container or brochure, should notify the patient tion and explain how to prevent it.

REFERENCES

1. Abbarah TR, Fredell JE, Ellenz GB: Ulceration by oral ferrous sulfate. JAMA 236 (20): 2320, 1976.
2. Agdal N: Drug-induced esophageal damage review and report of a fatal case of indomethacine-induced ulceration. Ugeskr Laeger 141: 3019-21, 1976.
3. Amendola MA, Spera TD: Doxycycline-induced esophagitis. JAMA 15, 253(7): 1009-11, 1985.
4. Bokey L, Hugh TB: Oesophageal ulceration associated with doxycycline therapy. Med J Aust 1(8): 236-7, 1975.
5. Cochrane P: Spontaneous esophageal rupture after carbachol therapy. Br Med J 1: 463-4, 1973.
6. Collins FJ, Mathews HR, Baker SE, Strakova JM: Drug-induced esophageal injury. Br Med J 1 (6179): 1673-6, 1979.
7. Crowson TD, Head LH, Ferrante WA: Esophageal ulcers associated with tetracycline therapy. JAMA 235 (25): 2747-8, 1976.
8. Ewans KT, Roberts GM: Where do all tablets go? Lancet 2: 1237, 1976.
9. Geschwind A: Oesophagitis and oesophageal ulceration ing ingestion of doxycycline tablets (letter). Med J Aust 140 (4): 223, 1984.
10. Heller SR, Fellows IW, Ogilvie AL, Atkinson M: Non-steroidal anti-inflammatory drugs and benign esophageal stricture. Br Med J (Clin Res) 285 (6336): 167-8, 1982.

[Downloaded from mjiri.iums.ac.ir on 2025-04-08]

11. Hey H, Jorgensen F, Sorensen K, Hasselbalch H, Wamberg T: Oesophageal transit of six commonly used tablets and capsules. Br Med J 285 (6356): 1717-19, 1982.
12. Kavin H: Oesophageal ulceration due to emepronium bromide (Letter). Lancet 1 (8008): 424-5, 1977.
13. Kikendall JW, Friedman AC, Oyewole MA, et al: Pill-induced esophageal injury— Case reports and review of the medical literature. Dig Dis Sci 28 (2): 174-82, 1983.
14. Mason SJ, O'Meara TF: Drug-induced esophagitis. J Clin Gastroenterol 3 (2): 115-20, 1981.
15. Pemberton J: Oesophageal obstruction and ulceration caused by oral potassium therapy. Brit Heart J 32:267-8, 1970.
16. Rosenthal T, Adar R, Militianu J, et al: Esophageal ulceration and oral potassium chloride ingestion. Chest 65: 463-5, 1974.
17. Sakai H, Seki H, Yoshidi Y, et al: Radiological study of drug-induced esophageal ulcer. Rinsho Hoshasen 25 (1): 27-34, 1980.
18. Schneider R: Doxycycline esophageal ulcers. Am J Dig Dis 22 (9): 805-7, 1977.
19. Teplick JG, Teplick SK, Ominsky SH, Haskin ME: Esophagitis caused by oral medication. Radiology 134 (1): 23-5, 1980.
20. Walta DC, Giddens JD, Johnson LF, et al: Localized proximal esophagitis secondary to ascorbic acid ingestion and esophageal motor disorder. Gastroenterology 70 (5 pt. 1): 766-9, 1976.

[Downloaded from mjiri.iums.ac.ir on 2025-04-08]

[Downloaded from mjiri.iums.ac.ir on 2025-04-08]