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Original article

Novel Endoscopic Therapy for the Treatment of Pill induced Esophageal ulcer

T.S. Chandrasekar, M. Murugesh, S. Radhakrishnan, M.A.C. Hameed Hussain, T. Sadagopan, J. Jeyaprakash, M.Ananthi.

SUMMARY

Background and aims; The available therapy for retrosternal pain and dysphagia associated with pill induced esophageal ulcer are only partially effective in relieving symptoms and no specific treatments have been shown to be beneficial in altering the course of medication induced injury. Our aim of the study is to assess the safety and efficacy of endoscopic injection of Lignocaine hydrochloride for the relief of retrosternal pain and dysphagia in cases of pill induced esophageal ulcer(s). Patients and methods; From March 2000 to March 2006, 17 patients of pill induced esophageal ulcer who did not respond to conventional treatment underwent endoscopic injection of Lignocaine hydrochloride using sclerotherapy needle in and around the pill induced esophageal ulcer(s) to relieve retrosternal pain and dysphagia. Relief of retrosternal pain and dysphagia with reference to Visual analogue scale (VAS) score and dysphagia grading respectively were scored by blinded examiners before and after treatment. Results: Of the 17 patients, 15 patients got immediate and complete relief of symptoms after the first session of injection and 2 patients had relief of dysphagia from grade 4 to grade 1- 2 after the first session of injection and appreciated complete relief of symptoms (dysphagia grade 0) after the second session of injection given 4 days later the first session of injection. There was significant change in VAS score before and after injection of Lignocaine hydrochloride ($p<0.0001$). Conclusions: The endoscopic injection Lignocaine hydrochloride in and around the pill induced esophageal ulcer(s) for the relief of odynophagia and retrosternal pain is safe and effective.

Key words: Pill induced esophageal ulcer, dysphagia, endotherapy, injection lignocaine hydrochloride

MedIndia Hospitals, Coimbatore, India.

Author for correspondence:

Dr. T.S.Chandrasekar, MD., DM, Chief Gastroenterologist, 96, Vivekananda Road, Ramnagar, Coimbatore 641009, e-mail: tscmedindia@gmail.com

INTRODUCTION

The pill induced esophagitis is an uncommon condition encountered in clinical practice. The presenting symptoms may range from mild retrosternal pain to severe odynophagia, retrosternal pain, burning sensation, and vomiting.[1]

The symptoms, particularly odynophagia, can be so severe in some as to necessitate hospitalisation and intravenous fluid administration and no specific treatments have been shown to be beneficial in altering the course of medication induced injury.[1] The available drugs Sucralfate, H2 receptor antagonists, Lignocaine viscous and Proton pump inhibitors administered orally for relief of odynophagia and retrosternal pain are ineffective[1]. These drugs have been tried empirically with the belief either suppressing the acidity, mucosal coating or local anesthetic effect. The site specific delivery of orally administered Lignocaine viscous is unpredictable which may be the reason for the limited efficacy.

As all of our patients presented with severe odynophagia and retrosternal pain, in spite of the conventional treatment mentioned earlier including oral Lignocaine viscous, they were not relieved of symptoms, We planned an endoscopic injection of Lignocaine hydrochloride using standard sclerotherapy needle in and around the midesophageal ulcer(s) associated with pill esophagitis. This case series evaluates the efficacy of Lignocaine hydrochloride injection for the the relief of pill induced dysphagia and retrosternal pain in 17 patients. This has not been reported till now to the best of our knowledge in the world literature.

PATIENTS AND METHODS

Patients

A total of 17 consecutive patients (11 men, 6 women; mean age 37years) were enrolled in the study between

March 2000 and September 2006. All the patients had a history of consumption of drugs implicated as the cause of pill induced esophagitis. 14 patients had taken Doxycycline hydrochloride and 2 patients had consumed Prednisolone orally and the remaining one patient had taken potassium chloride syrup. These drugs had been prescribed for various reasons.

The average duration of presentation was 6 days (range 2 to 10 days). The clinical presentations in our patients were severe dysphagia, retrosternal pain, retrosternal burning sensation and vomiting.

Informed consent for endoscopy and participation in this study was obtained from all patients. The institutional review board for human investigations of our hospital approved the clinical protocol for the study with written informed consent given by each patient before the procedure.

Instruments (Materials)

The instruments used in the study were as follows:

A standard videoendoscopy system, Olympus Optical Co., Ltd., Tokyo,

Japan), Lignocaine Hydrochloride Injection 1% (Astra Zeneca), and Sclerotherathy 23G needle (Boston scientific-Microvasive).

Methods

All the patients underwent complete haemogram, blood sugar, blood urea nitrogen, serum creatinine, electrocardiogram, chest radiography, cardiac evaluation and intradermal skin test for allergy to Lignocaine injection and all were fit for this study.

On presentation the patients marked the level of their pain on a 100 mm, non-hatched VAS scale[2]. It was predefined that patients with VAS pain scores of 30 mm or less would be categorised as having mild pain, those with scores of 70 mm or more were categorised as having severe pain and those from 31 mm to 69 mm as moderate pain.

The severity of dysphagia was graded according to a 5 point scale as follows; 0, able to consume a normal diet; 1, unable to swallow certain solid foods; 2, able to swallow semisolid soft foods; 3, only able to swallow liquids; 4, unable to swallow saliva.[3]

The endoscopic examinations were performed by an experienced single endoscopist. The esophagus, stomach, and duodenum were examined thoroughly. The lesions were described as esophageal ulcers either single or multiple. The stomach and duodenum appeared normal in all the patients.

All the patients with ulcers in the esophagus were given injection of 1%Lignocaine hydrochloride 0.5cc to 1cc per site in and around the esophageal ulcers. The procedure lasted over 10 to 20 minutes and all the patients received injection of Midazolam 0.06mg/kg prior to the procedure administered by an anesthetist and cardiac and respiratory monitoring were done during the procedure. The pre and post procedure symptom score evaluation was done by two blinded consultants, one prior to the injection and another after the injection therapy independent of the performing endoscopist.

Statistical analysis:

To compare the mean vas score between the groups, independent t test was employed and to find the effect of the treatment by injection of Lignocaine hydrochloride Paired t-test was used. Statistical package SPSS 10.0 was used for the analysis.

Results

Between March 2000 and September 2006, 17 patients (11male) of pill induced esophageal ulcer were given endoscopic injection of Lignocaine hydrochloride. The mean age of the patient was 37 years. 14 patients had taken Doxycycline Hydrochloride, 2 patients took Prednisolone orally and the remaining one patient had consumed syrup potassium chloride. Patients came after an average of 6 days after the onset of symptoms. Single large geographic ulcer measuring $\geq$1.5cm in the mid esophagus was seen in 12 patients and multiple small to medium sized ulcers measuring less than 1.5cm were seen in 5 patients.

Demographic data Table; 1

On admission,the patients included in the study were similar (since $P > 0.05$) with respect to age, sex and type of ulcer (Table 2).

Endoscopic injection of Lignocaine hydrochloride was given in all the patients as was there no relief from conventional treatment taken by them before presenting to us. The average amount of Lignocaine hydrochloride injection administered was 4.5ml in each patient and was there no complication except transient bradycardia in one patient during the procedure who recovered spontaneously.

It was observed that 10 out of 11cases (90%) in the grade 4 (unable to swallow saliva) and 5 out cases 6 (83%) in the grade 3 (able to swallow liquid) recovered to normal diet after the first session of treatment. (Table 3).

Table 1. Demographic, clinical and outcome details.

Patient Sl. No	Age / Sex	Drug inflicted	Retrosternal pain assessed by VAS in mm	Grade of Dysphagia	Type of Ulcer	Amount of Lignocaine Injected	Retrosternal pain assessed by VAS in mm after Lignocaine injection	Grade of dysphagia after Lignocaine injection	Follow up in months
1	35/M	Doxycycline	90	3	single	8 ml	0	0	8
2	32/F	Doxycycline	100	4	single	4ml	10	0	6
3	41/M	Doxycycline	100	4	single	6ml	0	0	9
4	30/M	Doxycycline	90	4	Multiple	10ml	5	0	15
5	28/F	Doxycycline	80	3	single	4ml	10	0	8
6	43/F	Syrup Pottassium chloride	90	4	single	5ml	5	0	12
7	30/M	Doxycycline	80	3	Multiple	10ml/2ml*	30	1	9
8	41/F	Doxycycline	90	3	single	4ml	15	0	10
9	29/M	Doxycycline	100	4	single	8ml	10	0	6
10	40/M	Doxycycline	100	4	single	6ml	5	0	18
11	38/M	Prednisolone	90	3	Multiple	8ml	0	0	14
12	38/F	Doxycycline	90	4	single	6ml	10	0	15
13	50/M	Doxycycline	100	4	Multiple	10ml	0	0	7
14	44/M	Doxycycline	80	4	Multiple	12ml/2ml*	40	2	8
15	39/M	Doxycycline	80	3	single	6ml	0	0	12
16	31/M	Doxycycline	100	4	single	6ml	10	0	12
17	40/F	Prednisolone	90	4	single	5ml	10	0	8

* *Sign indicates repeat injection*

Table 2. Mean VAS score value of the subjects before starting the treatment

Variable	N	Mean	SD	P-value
Sex				
Male	11	91.82	(8.74)	
Female	6	90.0	(6.32)	0.661
Type of Ulcer				
Single	12	92.5	(7.54)	
Multiple	5	88.0	(8.37)	0.294
Age Group				
≤ 38 yrs	9	91.11	(7.82)	
> 38 yrs	8	91.25	(8.35)	0.972

By applying paired t-test, it was observed that the difference of mean value of VAS in mm before and after treatment was statistically significant. Since P<0.0001, there was evidence to conclude that there is a significant reduction in mean score of VAS after treatment. (Table 4)

All these patients had a mean duration of follow up for10.4 months with a minimum period of 6 months with symptom questionnaire and none of the patient had any recurrence of symptoms during follow up and hence repeat endoscopy was not done.

DISCUSSION

Medication induced esophageal injury may occur at any age and with a variety of commonly used medications.[1] The incidence of pill esophagitis has been estimated as approximately four cases per 100,000 per year.[4] The first case of pill esophagitis was described in the English literature in1970[5]. Commonly implicated medications include Tetracycline's (especially Doxycycline), sustained-release Potassium preparations, nonsteroidal Anti-inflammatory drugs (NSAIDs) (especially Aspirin), Quinidine, Bisphosphonates and Emepronium bromide.[6]

The true incidence of pill esophagitis is probably still higher because of under-reporting, missed diagnoses, and

Table 3. Initial and final grade of improvement of all the subjects

	Grade after treatment						
Initial grade	**Normal Diet (Gr.0)**		**Unable to swallow solid food (Gr.1)**		**Able to swallow semisolid soft food (Gr.2)**		**Total**
	No.	**%**	**No.**	**%**	**No.**	**%**	**No.**
Able to swallow liquid (Gr.3)	5	83.3	1	16.7	6		
Unable to swallow saliva (Gr.4)	10	90.9	1	9.1	11		
Total	15	88.2	1	5.9	1	5.9	17

Table 4. Initial and final Mean VAS score value of all the subjects

Variable	N	Mean	SD	P-value
VAS score				
Initial	17	91.18	(7.81)	
Final	17	9.41	(10.88)	0.000

P<0.0001

subclinical episodes. Experts agree that there is an increase in incidence of pill esophagitis in the developed world because of the increasing age of the population and higher rates of prescription of drugs.[7]

The cornerstone of treatment is prompt discontinuation of the offending pill. 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[1]. 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.[1]

Because most cases of pill esophagitis are self-limited, mild or uncomplicated disease can be managed by simply discontinuing the medication and observing the patient. But in some the retrosternal pain and dysphagia can be severe requiring hospitalisation and further treatment. The currently available treatments for the relief of pain associated with pill induced esophagitis are Sucralfate, H2 receptor antagonists, Lignocaine viscous, and Proton pump inhibitors are ineffective and not standardized and approved by FDA[1]. Sucralfate binds to ulcerations in the esophagus caused by the pill. A Proton-Pump Inhibitor (PPI) or Histamine-2 (H_2) receptor antagonist is commonly used with the idea that reduction of acidity might help symptomatically.[1] 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.. The symptoms, particularly retrosternal pain and dysphagia, can be so severe and may require hospitalisation and intravenous fluid administration. Because of the inefficacy of available medications and lack of site specific delivery of these drugs, we have chosen to infiltrate the ulcers directly with Lignocaine hydrochloride. This was the first study reported in the world literature to the best of our knowledge, to show the efficacy of Lignocaine injection. Our study showed that endoscopic injection of 1% Lignocaine hydrochloride was effective in dramatic relief of symptoms. 15 out 17 patients got immediate relief of pain with one session of injection of Lignocaine Hydrochloride and the remaining 2 patients got complete relief with two sessions of injections of Lignocaine Hydrochloride with an interval of 4 days.

We anticipated the relief of dysphagia will be short lasting and symptoms might recur once the drug concentration and thereby the action wanes. To our surprise, all our patients showed total and permanent relief of dysphagia and retrosternal pain. We are not able to explain this observation and these findings may be the interesting aspect of our study.Probably the immediate relief of symptoms could have been due to the anesthetic effect and complete relief of symptoms could have been due to more site specific delivery of the local anesthetic agent relieving the perilesional neural irritation.

We hypothesize that the local anesthetic agent could have relieved the perilesional muscle spasm and there by promoting healing of mucosal ulcer which may explain the permanent and total relief of symptoms observed in our patients.

CONCLUSIONS

We conclude that this novel endoscopic injection of lignocaine hydrochloride therapy for relief of dysphagia

and retrosternal pain associated with pill induced esophagitis was safe and effective in relief of symptoms. The draw back of our study may be small number of cases and lack of randomization. Hence further studies are required in large numbers with randomization to confirm our findings.

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