

## Acute therapy with intravenous omeprazole on caustic esophageal injury: a prospective case series

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**SUMMARY.** The ingestion of caustic substances may result in significant esophageal injury. There is no standard treatment protocol for esophageal injury and most patients are treated with a proton pump inhibitor or H<sub>2</sub> antagonist. However, there is no clinical study evaluating the efficacy of omeprazole for caustic esophageal injury. A prospective study of 13 adult patients (>18 years of age) who were admitted to our hospital for caustic ingestion between May 2010 and June 2010 was conducted. Mucosal damage was graded using a modified endoscopic classification described by Zargar *et al.* Patients were treated with a proton pump inhibitor and maintained without oral intake until their condition was considered stable. Patients received omeprazole 80 mg in bolus IV, followed by continuous infusion of 8 mg/hour for 72 hours. A control endoscopy was performed 72 hours after admission. There was significant difference regarding endoscopic healing between the before and after omeprazole infusion ( $P = 0.004$ ). There was no hospital mortality at the follow-up. Omeprazole may effectively be used in the acute phase treatment of caustic esophagus injuries.

**KEY WORDS:** Omeprazole, caustic esophageal injury, treatment.

### INTRODUCTION

The ingestion of caustic substances induces a wide range of injuries to the gastrointestinal tract, which can be mild or fatal, or lead to chronic disease. Caustic agents with a pH level <2 or >12 rapidly penetrate layers of the esophagus resulting in necrosis-induced scar formation in the mucosa that limits deep tissue penetration.<sup>1</sup> The extent of tissue destruction depends on the physical form, type, and concentration of corrosive agent, premorbid state of the tissue, contact duration, and amount of substance ingested. Liquefaction necrosis occurs and serious esophageal injury becomes inevitable once alkaline liquids penetrate deep muscle layers.<sup>2</sup>

The basic histopathologic reaction of tissue subjected to caustic burn is the synthesis, deposition and remodeling of collagen and following full-thickness injuries to the esophageal wall, the normal esophagus is replaced by dense connective tissue. Consequently, when treating caustic burn injuries, it is necessary to prevent stenosis and inhibit collagen synthesis or change the properties of the deposited collagen. Collagen overproduction has been estimated to cause stenosis in half of the patients suffering severe burns.<sup>3</sup>

The main goal when treating caustic ingestion is the prevention of stricture formation.

The optimal management protocols applicable to treat severe damage after the ingestion of caustic substances remain controversial. The main purpose of medical treatment is the inhibition of any inflammatory reaction or stricture formation because of esophageal burning. Stricture formation is thought to be overcome by suppressing fibroplasia and scarring. Many agents directed at the pharmacological control of wound healing to prevent stricture formation have been used in previous experimental studies in the literature. Results of the treatment protocols including steroids, antibiotics, heparin, indomethacin, sucralfate, vitamin E, as well as total parenteral nutrition are controversial for corrosive burns.<sup>4–9</sup>

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Omeprazole is a proton pump inhibitor (PPI), which also has anti-inflammatory and antioxidant properties.<sup>10,11</sup> A few experimental studies have investigated the relationship between PPI and corrosive burns.<sup>8</sup> However, to our knowledge there is no information regarding human subjects. The aim of the present study was to evaluate the endoscopic and clinical effects of omeprazole in humans with corrosive esophageal burns.

## METHODS

A prospective study of 13 adult patients (>18 years of age) who were admitted to our hospital for caustic ingestion between May 2010 and June 2010 was conducted. The study protocol was approved by the local ethics committee of Ankara Education and Research Hospital within which the work was undertaken and conforms to the provisions of the Declaration of Helsinki in 1995 (as revised in Edinburgh 2000). In this study we included those admitted to emergency units because of complaints with accidental caustic ingestion. Oral feeding was entirely stopped at admission. Thirteen adult patients were included in the study with informed consent. Esophagogastroduodenoscopy (EGD) with a standard upper gastrointestinal endoscopy was performed by experienced physicians within 24 hours of ingestion. Endoscopes used were Pentax (Pentax Company, Tokyo, Japan). Oral cavity xylocaine spray was used for anesthesia. Mucosal damage was graded using a modified endoscopic classification described by Zargar *et al.* (Table 1).<sup>12</sup> After endoscopy was performed, patients were treated with a PPI and maintained without oral intake until their condition was considered stable. Patients received omeprazole 80 mg in bolus i.v., followed by continuous infusion of 8 mg/hour for 72 hours. A new endoscopy was performed 72 hours after admission. We obtained data of patient symptoms, organ involvement, mortality, and duration of hospitalization.

Demographic data were described by mean and standard deviations for normally distributed continuous variables, median and interquartile range for non-normally distributed continuous variables, and frequencies and percentages for categorical variables.

Chi-square tests adjusted for age obtained by generalized estimation equations were used to evaluate for overall survival.

## RESULTS

Thirteen consecutive patients (seven men; age 24 to 53 years) with caustic burn were admitted to our hospital between November 2009 and April 2010. Two patients' histories had systemic diseases (one patient's had essential hypertension and one patient's had diabetes mellitus). The other patients had no history of any diseases. Industrial cleaning agents containing lye or other alkaline chemical (i.e. caustic soda, drain cleaners, machine cleaners, and deacidification products containing sodium hydroxide or sodium-potassium hydroxide, dishwasher detergents) or caustic acids were considered caustic substances. The amount of ingested substance ranged from 2 to 75 mL (median 15 mL). Patients were admitted to hospital within median time of 3.5 hours (2 to 6 hours). According to endoscopic classification described by Zargar, there were three patients with grade 1, five patients with grade 2a, two patients with grade 2b, and two patients with grade 3 esophageal injuries. All patients' oral feeding was stopped first 72 hours and were given i.v. fluids. The patients were not prescribed any additional antibiotics or steroids. After omeprazole continuous infusion of 8 mg/hour for 72 hours, a repeat endoscopy demonstrated nine patients healed completely and the remaining three patients had grade 1 and one patient grade 3 esophageal injuries. There was significant difference regarding endoscopic healing between the before and after omeprazole infusion ( $P = 0.004$ ). After second endoscopy was performed, 12 patients revealed excellent recovery. These patients were started on oral feeding. However, one patients' second endoscopy showed grade 3 injury Zargar classification. Therefore, sucralfate suspension was started and we ordered prolonged nulla per os. There was no hospital mortality at the follow-up. Before and after omeprazole infusion endoscopic grading is shown in Figure 1. At admission and after treatment omeprazole treatment 13 patients' endoscopic imaging is shown in Figures 2 and 3.

After 1 year, we contacted these patients by telephone. Only one patient could not be reached by telephone who had grade 3a esophageal injury at both admission and second (72 hours after admission) endoscopy. Twelve patients questioned about their mortality, morbidity, hospitalization, and developed complications and expressed complaints. No mortality occurred within one year. Six patients had no complaints. The other six patients had endoscopy because of their complaints with heartburn, dyspepsia within 1 year. Their patients' endoscopies revealed that two patients had linear erosion of the

**Table 1** Zargar classification

|          |  |
|----------|--|
| Grade 0  | Normal examination   |
| Grade 1  | Edema and hypermia of the mucosa   |
| Grade 2a | Superficial ulceration, erosions, friability, blisters, exudates, hemorrhages, and whitish membranes         |
| Grade 2b | Grade 2a plus deep discrete/circumferential ulcerations  |
| Grade 3a | Small scattered areas of multiple ulceration and areas of necrosis with brown-black or grayish discoloration |
| Grade 3b | Extensive necrosis   |

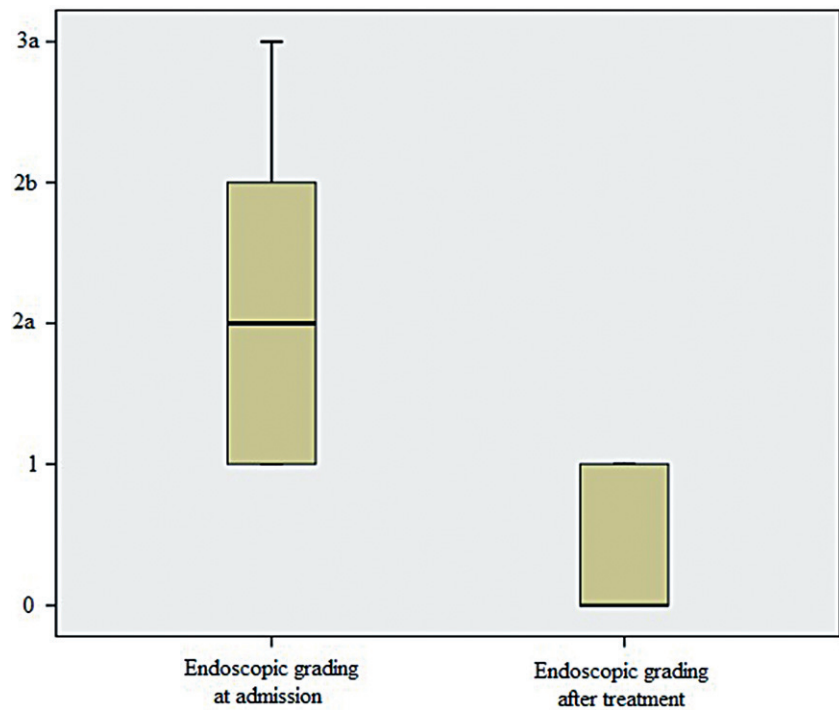


Fig. 1 Before and after endoscopic gradings of all 13 patients.

esophagus, and other patients have no esophageal injuries. All patients' follow-up are shown in Table 2.

DISCUSSION

Treatment of the acute corrosive intoxications includes: neutralization of corrosive agents, antibio-

tics, corticosteroids, antisecretory therapy, nutritional support, collagen synthesis inhibitors, esophageal dilation and stent placement, and surgery.<sup>13-15</sup> However, treatment of caustic burn is controversial. Intravenous PPIs, including omeprazole, have been used for either preventing or treating bleeding



Fig. 2 At admission, 12 patients' endoscopic imaging revealed grade 2b injury according to Zargar classification.

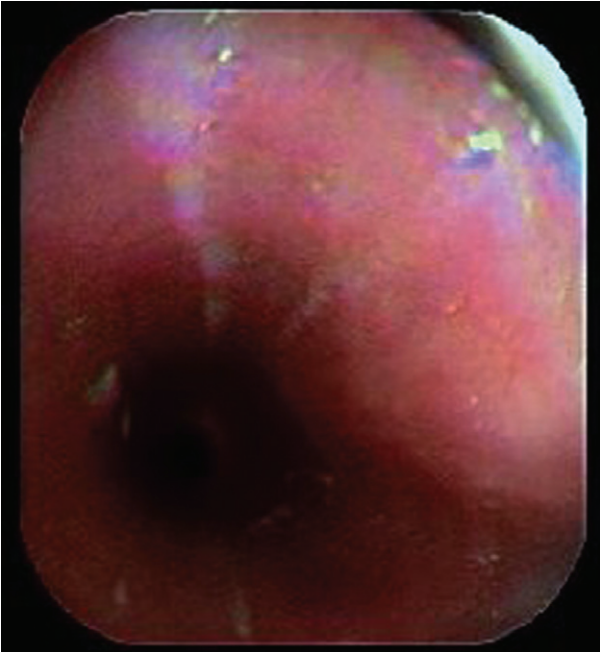


Fig. 3 After treatment omeprazole treatment, 12 patients' endoscopic imaging revealed grade 1 injury according to Zargar classification.

**Table 2** Demographic findings of the 13 patients

| Patient number | Age | Gender | Symptoms                     | Ingestion amount, mL | Zargar classification |                 |
|----------------|-----|--------|------------------------------|----------------------|-----------------------|-----------------|
|                |     |        |                              |                      | Before treatment      | After treatment |
| 1              | 24  | Male   | Dysphagia, heartburn, nausea | 75                   | 3a                    | 3a              |
| 2              | 42  | Female | Heartburn                    | 50                   | 2a                    | 0               |
| 3              | 28  | Male   | Heartburn                    | 10                   | 2a                    | 0               |
| 4              | 28  | Male   | No symptom                   | 10                   | 1                     | 0               |
| 5              | 32  | Female | Heartburn                    | 5                    | 1                     | 0               |
| 6              | 39  | Female | Heartburn                    | 25                   | 2a                    | 0               |
| 7              | 46  | Female | Burn of the throat           | 25                   | 2a                    | 0               |
| 8              | 30  | Female | Heartburn                    | 15                   | 2b                    | 1               |
| 9              | 53  | Male   | No symptom                   | 10                   | 1                     | 0               |
| 10             | 50  | Female | No symptom                   | 15                   | 2a                    | 0               |
| 11             | 33  | Male   | No symptom                   | 2                    | 1                     | 0               |
| 12             | 48  | Male   | Burn of the throat           | 10                   | 2b                    | 1               |
| 13             | 50  | Male   | Cough                        | 20                   | 3a                    | 1               |

gastrointestinal ulcers for a long time.<sup>16</sup> However, it has not been investigated for caustic esophageal injury before. In one experimental study, the efficacy of omeprazole on caustic burn was investigated.<sup>8</sup> Our study is the first study demonstrating that PPI infusion achieves effective improvement of endoscopic findings in 72 hours, and clinical significance of this is unknown based on data presented.

Omeprazole is a widely used antiulcer drug detected to protect against esophageal mucosal injury. It is a specific inhibitor of gastric H<sup>+</sup>/K<sup>+</sup>-ATPase. Moreover, PPIs accelerate apoptotic cell death selectively in cancer cells and significantly inhibit tumorigenesis and accelerate the microvascular and connective tissue regeneration. Possibly through an increase in the concentration of fibroblast growth factor, myofibroblasts change inhibition in lipid peroxidation and enhance the activities of catalase activity.<sup>11,17–19</sup> Furthermore, after treatment with omeprazole, hydroxyproline concentration in esophageal mucosa from patients with progressive systemic sclerosis decreases significantly.<sup>20</sup> Therefore, omeprazole might be protective in esophageal burns.

The role of acid in the persistent caustic ulceration in the esophagus and antrum was questioned, and the patient was empirically treated with PPI therapy. One experimental study has shown that omeprazole and vitamin E may prevent inflammation in the early phase of corrosive burn and thereby scar formation in the late phase of wound healing of the esophagus following the ingestion of acid and/or alkali.<sup>8</sup>

The most common complications of caustic injuries that may appear are: perforation, gastrointestinal bleeding, sepsis, esophageal strictures and stenosis, stenosis of gastric antrum and pylorus, and cancer of the esophagus and the stomach. Endoscopically visualized esophageal injury has been shown to be predictive of complications of caustic ingestion. Generally, patients with grades 0, 1, or 2A injury escape with no sequelae. Patients with grade 2B to 3 injury have

a high rate of developing strictures. Patients with grade 3 injury are at risk for both systemic complications requiring intensive care unit admission and local complications of bleeding and perforation. Most deaths occur in patients with grade 3 injury.<sup>12,21,22</sup> Our study showed that endoscopic complete healing even in one patient with grade 3 was achieved in all cases following continuous PPI infusion. Larger case series including more patients with grade 2b and 3 caustic burns would further clarify the efficacy of PPI infusion.

In conclusion, gastric acid suppression with PPIs seems to be efficient for treating corrosive burn injury of the esophagus. This is a preliminary observation of i.v. PPI; further study is needed. Based on this current study, a future randomized, placebo-controlled study should be designed to determine if PPI truly makes a difference.

## References

- Schneider S, Wax P. Caustics. In: Marx J, Hockberger R, Walls R (eds). *Rosen's Emergency Medicine: Concepts and Clinical Practice*, 5th edn. St. Louis, MO: Mosby, 2002; 2115–19.
- Caustic M W R. Ingestions: pathophysiology, diagnosis, and treatment. *Clin Pediatr* 1986; 25: 192–6.
- Nayci A, Cakmak M, Renda N, Ereku S. The effect of corticosteroids and pentoxifylline in inhibition of wound healing in corrosive esophageal burns: a prospective randomised trial in rats. *Int J Surg* 1997; 82: 371–5.
- Fulton J A, Hoffman R S. Steroids in second degree caustic burns of the esophagus: a systematic pooled analysis of fifty years of human data: 1956–2006. *Clin Toxicol (Phila)* 2007; 45: 402–8.
- Broto J, Asensio M, Jorro C S *et al.* Conservative treatment of caustic esophageal injuries in children: 20 years of experience. *Pediatr Surg Int* 1999; 15: 323–5.
- Bingöl-Kologlu M, Tanyel F C, Müftüoğlu S *et al.* The preventive effect of heparin on stricture formation after caustic esophageal burns. *J Pediatr Surg* 1999; 34: 291–4.
- Temir Z G, Karkiner A, Karaca I, Ortaç R, Özdamar A. The effectiveness of sucralfate against stricture formation in experimental corrosive esophageal burns. *Surg Today* 2005; 35: 617–22.
- Topaloglu B, Bicakci U, Tander B *et al.* Biochemical and histopathologic effects of omeprazole and vitamin E in rats



- with corrosive esophageal burns. *Pediatr Surg Int* 2008; 24: 555–60.
- 9 Pul M, Yılmaz N, Deger O, Gürses N. Indomethacin for prevention of stricture formation due to alkali-induced corrosive esophageal burns in the rat. *Pediatr Surg Int* 1990; 5: 416–17.
  - 10 Bicakci U, Tander B, Ariturk E, Aydin B K. Effects of omeprazole and gentamicin on the biochemical and histopathological alternations of the hypoxia/reoxygenation induced intestinal injury in newborn rats. *Pediatr Surg Int* 2005; 21: 800–5.
  - 11 Biswas K, Bandyopadhyay U, Chattopadhyay I, Varadaraj A. A novel antioxidant and antiapoptotic role of omeprazole to block gastric ulcer through scavenging of hydroxyl radical. *J Biol Chem* 2003; 278: 10993–1001.
  - 12 Zargar S A, Kochhar R, Mehta S, Mehta S K. The role of fiberoptic endoscopy in the management of corrosive ingestion and modified endoscopic classification of burns. *Gastrointest Endosc* 1991; 37: 165–9.
  - 13 Zabalegui A, Miján de la Torre A, Sáez-Royuela F, López Morante A, Yuguero del Moral L, Ojeda Giménez C. Severe gastroesophageal lesions due to caustics: the role of nutritional support. *Nutr Hosp* 1995; 10: 364–7.
  - 14 Arbell D, Udassin R, Koplewitz B Z *et al.* Prevention of esophageal strictures in a caustic burn model using halofuginone, an inhibitor of collagen type I synthesis. *Laryngoscope* 2005; 115: 1632–5.
  - 15 Han Y, Cheng Q S, Li X F, Wang X P. Surgical management of esophageal strictures after caustic burns: a 30 years of experience. *World J Gastroenterol* 2004; 10: 2846–9.
  - 16 Bardou M, Martin J, Barkun A. Intravenous proton pump inhibitors: an evidence-based review of their use in gastrointestinal disorders. *Drugs* 2009; 69: 435–48.
  - 17 Kim Y J, Lee J S, Hong K S, Chung J W, Kim J H, Hahm K B. Novel application of proton pump inhibitor for the prevention of colitis-induced colorectal carcinogenesis beyond acid suppression. *Cancer Prev Res (Phila)* 2010; 3: 963–74.
  - 18 Arisawa T, Harata M, Kamiya Y *et al.* Is omeprazole or misoprostol superior for improving indomethacin-induced delayed maturation of granulation tissue in rat gastric ulcers? *Digestion* 2006; 73: 32–9.
  - 19 Kil B J, Kim I W, Shin C Y *et al.* Comparison of IY81149 with omeprazole in rat reflux oesophagitis. *J Auton Pharmacol* 2000; 20: 291–6.
  - 20 Hendel L. Hydroxyproline in the oesophageal mucosa of patients with progressive systemic sclerosis during omeprazole-induced healing of reflux oesophagitis. *Aliment Pharmacol Ther* 1991; 5: 471–80.
  - 21 Zargar S A, Kochhar R, Nagi B, Mehta S, Mehta S K. Ingestion of corrosive acids. Spectrum of injury to upper gastrointestinal tract and natural history. *Gastroenterology* 1989; 97: 702–7.
  - 22 Zargar S A, Kochhar R, Nagi B, Mehta S, Mehta S K. Ingestion of strong corrosive alkalis: spectrum of injury to upper gastrointestinal tract and natural history. *Am J Gastroenterol* 1992; 87: 337–41.