Steroids for the Treatment of Corrosive Esophageal Injury:

A Statistical Analysis of Past Studies

JOHN M. HOWELL, MD, FACEP,*
WILLIAM C. DALSEY, MD, FACEP,†
F. WRIGHT HARTSELL, MD,‡ CLIFFORD A. BUTZIN, PHD§

Caustic esophageal injury causes substantial morbidity and mortality. However, the use of corticosteroids to treat this problem has been evaluated in a limited number of studies because adequate sample size is difficult to obtain. We analyzed 361 subjects with corrosive esophageal injury derived from 10 retrospective and three prospective publications. We divided cases into those treated with corticosteroids and antibiotics (T) and those that received neither modality (NT) based on inclusion and exclusion criteria. Forty-one percent of NT cases developed esophageal stricture and 19% of T cases developed this complication ($P < .01$). There were no reported strictures among 72 first-degree esophageal burns (combined T and NT cases). The T group contained 54 strictures among 228 patients (24%) with either second- or third-degree burns. The NT group of 25 patients with the same burn severity suffered 13 strictures (52%) ($P < .01$). Reports of death and gastrointestinal hemorrhage did not increase among steroid-treated patients. We do not recommend corticosteroid therapy for first-degree esophageal injuries. However, this therapy may be useful in preventing strictures among patients with second- or third-degree corrosive esophageal burns. (Am J Emerg Med 1992; 10:421-425. Copyright © 1992 by W.B. Saunders Company)

The incidence of caustic ingestion in the United States approaches 26,000 per year.[1] Toxic exposures of this type persist despite legislation to limit the availability of concentrated liquid and solid caustics. Once ingested, potent caustics may impart full-thickness esophageal necrosis within minutes.[2-4] The body subsequently heals itself by lying down collagen, which promotes esophageal stricture formation over the following weeks, months, and years. Once formed, esophageal strictures are difficult to treat and constitute significant morbidity. Stricture prevention is one of the primary goals of therapy. Since 1950, when Spain et al[5] documented that steroids suppress inflammation in mice, corticosteroids have been the mainstay of treatment for serious caustic injuries of the esophagus. However, various animal and clinical human studies since that time failed to prove definitively that steroids, when delivered parenterally or by mouth, prevent esophageal strictures.

We reviewed 361 cases of caustic ingestion with documented esophageal injury extracted from studies published in the English literature since 1956.[6-18] We statistically analyzed data to determine what effect, if any, steroids and concomitant antimicrobials had on esophageal stricture rates when compared with a cohort not treated with steroids and antimicrobials.

METHODS

We reviewed prospective and retrospective human reports of steroid therapy for caustic esophageal injury published in the English literature between 1956 and 1991. We used Grateful Med for the Macintosh, version 1.5 (National Library of Medicine) for citations between 1966 and 1991, and Index Medicus for citations after 1956 to locate publications based on the medical subject headings and key words "caustic," "alkali," "acid," and "esophagus." We then reviewed additional citations based on the reference sections of publications obtained through Grateful Med and Index Medicus.

According to predetermined inclusion and exclusion criteria, we extracted 361 cases of adult and pediatric corrosive ingestion from more than 2,000 reported cases.[6-18] All but three studies were retrospective.[6,13,16] Inclusion criteria were (1) esophageal injury documented by esophagoscopy or exploratory surgery and (2) patient management either with no steroid and antimicrobial treatment or with at least a 2-week course of steroids and antimicrobials. We chose a 2-week duration of corticosteroid therapy to assess the effects of suppression of the inflammatory response during active fibroblast proliferation, which occurs by that time.[3] We excluded survivors with either fourth-degree injuries (ie, perforation) or partial treatment defined as less than 2 weeks of steroids and antimicrobials. We also excluded subjects in whom esophageal damage was presumed but not documented by esophagoscopy or surgery, regardless of treatment. Table 1 lists selected articles excluded from analysis. This does not constitute the full list of excluded articles, only those human studies that merited consideration relative to our inclusion and exclusion criteria. Clinical reviews and animal experiments were excluded but not listed in Table 1.

We derived the steroid treatment (T) group of 283 subjects from nine retrospective[8-12,14,15,17,18] and two prospective[6,13] publications. Three retrospective[7,8,15] and three prospective[6,13,16] publications contained 78 subjects that formed the no treatment (NT) group. Two prospective studies[6,13] examined the effectiveness of steroid and antimicrobial therapy

From the *Department of Emergency Medicine, Georgetown University Hospital, Washington, DC; the †Department of Emergency Medicine, Albert Einstein Medical Center, Philadelphia, PA; and the ‡Emergency Department and the §Clinical Investigation Directorate, Wilford Hall USAF Medical Center, Lackland Air Force Base, San Antonio, TX.

Manuscript received November 18, 1991; revision accepted April 6, 1992.

The opinions or assertions contained herein are the private views of the authors and are not to be construed as official or as reflecting the views of the US Air Force or the Department of Defense.

Reprints not available.
Key Words: Caustic, alkali, esophagus.

0735-6757/92/1005-0005$5.00/0

TABLE 1. Selected Articles Excluded From Statistical Consideration Followed by the Reasons for Exclusion

Cleveland WW, Thornton N, Chesney JG, et al: The effect of prednisone in the prevention of esophageal stricture following the ingestion of lye. South Med J 1958;51:861-864 (esophagoscopy not consistently performed)

Feldman M, Iben AB, Hurley EJ: Corrosive injury to oro-pharynx and esophagus: Eighty five consecutive cases. Calif Med 1973;118:6-9 (stricture rates not reported)

Ferguson MK, Migliore M, Staszak VM, et al: Early evaluation and therapy for caustic esophageal injury. Am J Surg 1989;157:116-120 (duration of treatment not clear; not clear if all untreated patients were endoscopied)

Gandhi RP, Cooper A, Barlow BA: Successful management of esophageal strictures without resection or replacement. J Pediatr Surg 24:745-750 (intralesional steroids)

Kirsh MM, Peterson A, Brown JW, et al: Treatment of caustic injuries of the esophagus: A ten year experience. Ann Surg 1978;188:675-678 (antibiotics administered alone and limited results)

Meredeth JW, Kon ND, Thompson JN: Management of injuries from lipid lye ingestion. J Trauma 1988;28:1173-1180 (antibiotics administered alone)

Middlekamp JN, Cone AJ, Ogura JH, et al: Ensoscopic diagnosis and steroid and antibiotic therapy of acute lye burns of the esophagus. Laryngoscope 1961;71:1354-1361 (results may have been included in later paper)

Ray ES, Morgan DL: Cortisone therapy of lye burns of the esophagus. J Pediatr 1956;49:394-397 (many patients received only 7-day course of steroids)

Ritter FN, Gago O, Komorn RM: The rationale of emergency esophagogastrectomy in the treatment of liquid caustic burns of the esophagus and stomach. Ann Otol 1974;80:513-520 (small number of cases incompletely described)

Sarfati E, Gossot D, Assens P, et al: Management of caustic ingestion in adults. Br J Surg 1987;74:146-148 (antibiotics administered alone)

Wijburg FA, Heymans HSA, Urbanus NAM: Caustic esophageal lesions in childhood: Prevention of esophageal stricture formation. J Pediatr Surg 1989;24:171-173 (used a stent)

Yarington CT, Bales GA, Frazer JP: A study of the management of caustic esophageal trauma. Ann Otol 1964;73:1130-1135 (variable period of steroid treatment; results not consistently presented)

Zargar SA, Kochhar R, Mehta S, et al: The role of fiberoptic endoscopy in the management of corrosive ingestion and modified endoscopic classification of burns. Gastrointest Endosc 1991;37:165-169 (method of treatment not elucidated)

compared with untreated cohorts in a randomized fashion. The third prospective study[16] evaluated the role of fiberoptic endoscopy in acute caustic ingestion; however, we retrieved data concerning only untreated first-degree injuries from this article. Retrospective publications[7-12,14-18] reported nonrandomized, uncontrolled case series data regarding therapy of caustic esophageal injury (ie, not case-control methodology). However, only data that met inclusion and exclusion criteria were included in this study. One retrospective[8] and two prospective[6,13] publications reported both T and NT cases. Cases taken from the remaining publications[7,9-12,14-18] pertained exclusively to one treatment method or the other. Four publications[7,8,12,17] did not differentiate first-, second-, and third-degree esophageal burns (64 cases). The majority of substances ingested were alkali, and the remainder included acids, detergents, bleaches, ammonia, and organic phosphorus compounds.

On the basis of descriptions in each publication, we placed esophageal injuries into one of two diagnostic categories: (1) first-degree and (2) combined second- and third-degree burns. One study descriptively represented the extent of esophageal injury as ulcerative[10] (120 cases). We included these subjects in the combined second- and third-degree subheading (Table 2) because they are consistent with definitions regarding the depth of injury and appearance of second- and third-degree caustic esophageal burns already described.[6,19-22] Burns characterized as "severe" in one publication[9] (seven cases) were presumed to be third-degree because they represented esophageal lesions graded on a scale of "mild," "moderate," and "severe."

We extracted information concerning deaths from six of 13 studies.[7,11,13-15,17] Deaths were not included when calculating stricture rates for T and NT groups. Expirations were considered separately since treatment duration was not clear for most cases when patients died during the course of therapy. We evaluated data with the Pearson chi square test and set alpha at 0.01.

RESULTS

There was inadequate information to compare T and NT groups except in broad terms regarding pediatric and adult classifications reported by each group of investigators. Table 3 lists percentages of pediatric subjects; "children" were described as those younger than 15 to 17 years of age. The ages of all subjects ranged between 3 months and 69 years. Steroids used included prednisone, prednisolone, methylprednisolone, cortisone, and hydrocortisone. Tetracycline, ampicillin, penicillin, streptomycin, and chloramphenicol were used as antimicrobials. Thirty-two of 78 NT cases (41%) developed esophageal strictures. In comparison, 53 of 283 (19%) T cases developed strictures ($P < .01$). No strictures were reported among 72 first-degree injuries. Fewer strictures occurred in the T group made up of combined second- and third-degree burns ($P < .01$) (Table 2). Six studies listed 13 deaths related to caustic ingestion (Table 4).[7,11,13-15,17] Steroid treatment did not increase the incidence of either death or gastrointestinal hemorrhage.

DISCUSSION

Ingested corrosives impart esophageal burns severe enough to cause stenosis and a chronic inability to transmit food. The result is devastating and manifested by chronic

TABLE 2. Strictures Among Nontreated and Steroid-Treated Subjects With First-, Second-, and Third-Degree Esophageal Burns

	First-Degree	Second- and Third-Degree
Treatment	0/49 (0%)	54/228 (24%)
No treatment	0/23 (0%)	13/25 (52%)
P value	NS	<.01

Note: The first number in each grouping represents the number of strictures among the total patients in that subset, represented by the second number.

TABLE 3. Description of Studies Included in Analysis

Ref	Publication Date	Study Type	Steroids Used	Percentage of Children	Steroid-Treated (No. of Strictures/ Total No. of Patients)			Not Treated (No. of Strictures/ Total No. of Patients)		
					First-Degree	Second- and Third-Degree	Total	First-Degree	Second- and Third-Degree	Total
Alford and Harris[7]	1959	Retrospective	Untreated	67						17/28
Anderson et al[6]	1990	Prospective	Prednisolone	100	0/6	10/25	10/31	0/13	11/16	11/29
Bikhazi et al[8]	1969	Retrospective	Not reported	77			5/19			2/2
Cannon and Chandler[9]	1963	Retrospective	Prednisolone	71	0/3	3/28	3/31			
Cardona and Daly[10]	1971	Retrospective	Cortisone, prednisolone	100		13/120	13/120			
Estrera et al[11]	1986	Retrospective	Not reported	35	0/2	5/7	5/9			
Haller et al[12]	1971	Retrospective	Prednisolone	100			5/9			
Hawkins et al[13]	1980	Prospective	Methylprednisolone	0		4/11	4/11		2/9	2/9
Middlekamp et al[14]	1969	Retrospective	Cortisone, prednisolone, hydrocortisone, methylprednisolone	100	0/19	8/13	8/32			
Moazam et al[18]	1987	Retrospective	Not reported	100	0/15		0/15			
Schild[17]	1985	Retrospective	Prednisolone	0			3/6			
Showkat et al[16]	1991	Prospective	Untreated	0.04				0/10		0/10
Webb et al[15]	1970	Retrospective	Prednisolone	71	0/4	11/24	11/18			
Totals					0/49	54/228	53/283	0/23	13/25	32/78

pain, malnutrition, and the need for multiple surgical procedures. Many clinicians use steroids to prevent stricture formation, but the effectiveness of this treatment is unproved due to a lack of statistical power among prospective studies.[6,13] The largest prospective study to date found that all steroid-treated subjects suffered 5.7% fewer strictures[6]; however, sample size was limited in this 18-year controlled study.

TABLE 4. Causes of Death Related to Type of Treatment

	No. of Deaths (%)
No Steroid or Antimicrobial Therapy	
Spontaneous esophageal perforation	1
Perforation at esophagogastrectomy site	1
Esophageal perforation during dilation	1
Abdominal viscus perforation and aspiration	1
Peritonitis	1
Fatal hemorrhage	1
Aspiration pneumonia	1
Total no. of patients	7
Steroid and antimicrobial therapy	
Severe esophagogastric necrosis	4
Fatal hemorrhage	
Milk aspiration with tracheostomy in place	1
Severe esophageal stenosis and refusal to eat; died 10 weeks postinjury	1
Total no. of patients	6
Miscellaneous	
Spontaneous esophageal perforation after receiving one dose of steroids	1

Bleaches and nonindustrial detergents impart superficial first-degree injuries. Our results are consistent with those of Anderson et al[6] in that we found no strictures among 72 patients with first-degree esophageal burns. In all cases, untreated patients with first-degree burns healed without strictures and the use of steroids did not alter these results. The clinical prognosis of isolated first-degree burns is excellent and should result in complete healing with or without the use of corticosteroids.

Patients with circumferential second- and third-degree esophageal burns have a substantial risk of developing esophageal strictures. We identified a statistically significant improvement in the stricture rate for the T group of combined second- and third-degree esophageal burns. The difference between T and NT groups for second- and third-degree burns approximates the findings of Anderson et al.[6] We were unable to statistically analyze isolated second- and third-degree categories because several investigators combined these patients into one group for the purpose of analysis. Prospective data suggest that most patients with third-degree burns develop esophageal strictures regardless of therapy.[6,13] Therefore, it is possible that the difference we noted between T and NT groups for combined second- and third-degree injuries is due to an isolated treatment effect in the second-degree cohort.

Many vilify the use of steroids after caustic ingestion based on concerns regarding sepsis, gastrointestinal perforation, and hemorrhage. However, we found no increase in the number of deaths or morbid complications among treated patients. Selected investigators reported no deaths among steroid-treated patients. Septic complications not resulting in deaths were not consistently reported in the publications

we reviewed and could represent unreported morbidity. However, our analysis suggests there is no increase in morbidity or mortality among steroid-treated patients.

Weaknesses of our study relate to the analysis of combined, retrospective case series data from multiple studies. Comparing T and NT groups was problematic because complete information was unavailable in most publications. We did not adequately control subject profiles, use of early surgery, time to endoscopy, and time to steroid administration. Steroids and antibiotics used varied from study to study, although each study in the T group used steroids and antimicrobials for at least 2 weeks. Further, the end points chosen were straightforward: esophageal stricture and death. Follow-up was not uniform and varied from 6 months to several years. However, in all studies follow-up was adequate to detect substantial numbers of strictures in each cohort. Deaths may have been underreported because they were discussed in less than half of the publications.

Due to strict inclusion and exclusion criteria, only 361 cases were included after reviewing more than 2,000 cases. This stringent selection process may have caused selection bias. For example, we included more children than adults. However, we are unaware of differences between adults and children related to untreated stricture rates or response to steroid therapy in this clinical setting. The number of NT patients is smaller than those in the T group. However, it is possible that unpublished NT patients were predominantly those who developed strictures because steroid therapy has been considered effective by many investigators. Consequently, the complication rate among NT patients may be lower than a "true" sample, and we detected a significant difference between T and NT cases. Publication bias may have occurred because only the English literature was reviewed. Caustic ingestion occurs with some frequency in adults from Malaysia and Far East. A final drawback of our study, and of all publications treating this subject to date, is a lack of attention to esophageal function as outcome. Cardona and Daly[10] mentioned that steroid-treated esophageal tissue appeared more pliable than untreated tissue. However, none of the studies approached functional recovery after esophageal stricture in a systematic, quantitative manner. We believe functional recovery is the goal of therapy and this should be the measured outcome when evaluating potential treatments.

Although it occurs infrequently, caustic esophageal stenosis wreaks anatomic and psychological havoc. Therefore, small differences in stricture rates after given methods of treatment may be clinically significant. Statistically powerful prospective analysis is problematic due to the inherent difficulty in obtaining adequate sample size. Prospective, control matched trials, both animal and human, are needed to further clarify this issue.

Analysis of the data suggests that combined steroid and antimicrobial therapy in patients with second- or third-degree esophageal burns may significantly decrease the incidence of esophageal stricture formation without increasing morbidity or mortality. Corticosteroids may decrease the possibility of strictures in some patients, but will not prevent them in all such individuals. Alternative treatment regimens that further improve outcome should be explored and larger prospective studies of this clinical issue are needed.

CONCLUSION

Caustic substances lead to extensive esophageal necrosis and subsequent stricture formation when ingested in sufficient quantities and concentrations. We statistically analyzed 361 subjects with corrosive esophageal injury derived from 13 publications. There were no strictures reported among all cases with first-degree esophageal burns. In the combined steroid- and antibiotic-treated group, we noted 54 strictures among 228 patients (24%) with either second- or third-degree burns. The nontreatment group of 25 patients with similar burn severity suffered 13 strictures (52%) ($P < .01$). We do not recommend corticosteroid therapy for the treatment of first-degree esophageal injuries. Prospective clinical trials with adequate sample sizes are needed to further evaluate the role of steroids in preventing strictures among patients with second- and third-degree corrosive esophageal burns.

REFERENCES

1. Lovejoy FH: Corrosive injury of the esophagus in children: Failure of corticosteroid treatment reemphasizes prevention. N Engl J Med 1190;323:668-670

2. Kirsh MM, Ritter F: Caustic ingestion and subsequent damage to the oropharyngeal and digestive passages. Ann Thorac Surg 1976;21:74-82

3. Haller JA, Jr, Bachman K: The comparative effect of current therapy on experimental caustic burns of the esophagus. Pediatrics 1964;34:236-245

4. Ashcraft KW, Padula RT: The effect of dilute corrosives on the esophagus. Pediatrics 1974;53:226-232

5. Spain DM, Molomut N, Haber A: The effect of cortisone on the formation of granulation tissue in mice. Am J Pathol 1950; 26:710-711

6. Anderson KD, Rouse TM, Randolph JG: A controlled trial of corticosteroids in children with corrosive injury of the esophagus. N Engl J Med 1990;323:637-640

7. Alford BR, Harris HH: Chemical burns of the mouth, pharynx and esophagus. Ann Otol 1959;68:122-128

8. Bikhazi HB, Thompson ER, Shumrick DA: Caustic ingestion: Current status. Arch Otolaryngol 1969;89:112-115

9. Cannon S, Chandler JR: Corrosive burns of the esophagus: Analysis of 100 patients. Eye Ear Nose Throat Mon 1963; 42:35-44

10. Cardona JC, Daly JF: Current management of corrosive esophagitis: An evaluation of results in 239 cases. Ann Otol 1971;80:521-527

11. Estrera A, Taylor W, Mills LJ, et al: Corrosive burns of the esophagus and stomach: A recommendation for an aggressive surgical approach. Ann Thorac Surg 1986;41:276-283

12, Haller JA, Andrews HG, White JJ, et al: Pathophysiology and management of acute corrosive burns of the esophagus: Results of treatment of 285 children. J Pediatr Surg 1971;6:578-583

13. Hawkins DB, Demeter MJ, Barness TE: Caustic ingestion: Controversies in management: A review of 214 cases. Laryngoscope 1980;90:98-108

14. Middlekamp JN, Ferguson TB, Roper CL, et al: The management and problems of caustic burns in children. J Thorac Cardiovasc Surg 1969;57:341-347

15. Webb WR, Koutras P, Ecker RR, et al: An evaluation of steroids and antibiotics in caustic burns of the esophagus. Ann Thorac Surg 1970;9:95-102

16. Showkat AZ, Kochhar R, Mehta S, et al: The role of fi-

beroptic endoscopy in the management of corrosive ingestion and modified endoscopic classification of burns. Gastrointest Endosc 1991;37:165-169

17. Schild JA: Caustic ingestion in adult patients. Laryngoscope 1985;95:1199-1201

18. Moazam F, Talbert JL, Miller D, et al: Caustic ingestion and its sequelae in children. South Med J 1987;80:187-190

19. Kirsh MM, Ritter F: Caustic ingestion and subsequent damage to the oropharyngeal and digestive passages. Ann Thorac Surg 1976;21:74-82

20. Kirsh MM, Peterson A, Brown J, et al: Treatment of caustic injuries of the esophagus: A ten year experience. Ann Surg 1978;188:675-678

21. Knopp R: Caustic ingestions. JACEP 1979;8:329-336

22. Range DR, Hirokawa RH, Bryarly RC: Caustic ingestion. Ear Nose Throat J 1983;62:46-63