Predictors of Esophageal Stricture in Children with Unintentional Ingestion of Caustic Agents

Tsung-Yi Chen, MD; Sheung-Fat Ko[1], MD; Jiin-Haur Chuang[2], MD; Hsin-Wei Kuo[3], MD; Mao-Meng Tiao, MD

Background: Prediction of the severity of esophageal injury following ingestion of a caustic substance is a challenging problem for clinicians. It was hoped that risk factors for the early prediction of esophageal stricture in such patients could be identified in this study.

Methods: This study comprises an evaluation of 32 children with esophageal injury due to ingestion of caustic materials. Patients' signs and symptoms as well as laboratory data including leukocyte counts and C-reactive protein level were reviewed.

Results: Patients who presented with a greater number of symptoms and signs were inclined to have more severe esophageal injury and stricture. The frequency of symptoms and signs in patients with serious esophageal injury was higher than that in patients with low-grade injury. Patients with severe injury were more significantly associated with the occurrence of stricture. The characteristic of caustic ingestion was associated with esophageal stricture, but not esophageal injury. There was no statistically significant difference in leukocyte counts relative to severity of esophageal injury. The mean of leukocyte counts of patients with esophageal stricture was close to that of patients without esophageal stricture. There was also no statistically significant difference in C-reactive protein values between the 2 groups of patients.

Conclusions: Leukocyte counts and C-reactive protein are not useful parameters for predicting the severity of esophageal injury and occurrence of stricture following injury to the esophagus by caustic materials. Alkali ingestion more probably leads to esophageal stricture than acid ingestion. After caustic ingestion, the presence of a greater number of symptoms and signs suggests a more-severe injury, which necessitates more-aggressive management.
(Chang Gung Med J 2003;26:233-9)

Key words: **leukocyte, C-reactive protein, caustic, esophagus, stricture.**

Caustic materials are useful but constitute a potential public health risk. Legislation to limit the concentrations of hazardous cleaners and to ensure that containers are childproof has been advocated for a long time.(1) Unfortunately, accidental ingestion among children remains common. The incidence of

From the Department of Pediatrics, [1]Department of Radiology, [2]Department of Pediatric Surgery, Chang Gung Children's Hospital, Kaohsiung, Chang Gung University; [3]Department of Internal Medicine, Kaohsiung Medical University Hospital, Kaohsiung.
Received: Sep. 17, 2002; Accepted: Jan. 9, 2003
Address for reprints: Dr. Mao-Meng Tiao, Department of Pediatrics, Chang Gung Children's Hospital. 123, Dabi Road, Niaosung Shiang, Kaohsiung, Taiwan 833, R.O.C. Tel.: 886-7-7317123; Fax: 886-7-7338009; E-mail: tsungyi@ms30.url.com.tw

these accidents was estimated to be as high as 15.8/100,000 per year.[2] Prediction of the presence and severity of esophageal injury following ingestion of a caustic substance is a challenging problem for the clinician. The use of initial symptoms and signs to predict the outcome of esophageal injury is controversial.[3-5] Furthermore, whether initial symptoms and signs are useful in assessing the degree of esophageal injury by endoscopy is still contentious.[3,6] In this retrospective review, we evaluated the correlation between the initial clinical presentations and the severity of esophageal injury and the occurrence of stricture.

METHODS

From 1986 to 2000, 38 children with a history of caustic ingestion who were admitted to our hospital were included. There was no history of reflux esophagitis in any of our patients. Excluded from evaluation were 6 patients who did not have endoscopy, those with unstable vital signs, and those for whom parental consent could not be obtained. The patients' age, symptoms, the type and character of the caustic agent, and prognosis were reviewed. Inflammatory parameters such as leukocyte counts and C-reactive protein (CRP) of the first blood sample after admission were also reviewed. Also evaluated were 6 common manifestations of caustic ingestion: fever, vomiting, oropharyngeal burn, drooling or dysphagia, abdominal pain or refusal to eat, and respiratory distress.[3,5] The amount of caustic material ingested was not reviewed because it was ambiguously expressed (e.g., a sip, a gulp, a spoonful, or a cup).

Endoscopy was performed between 12-48 hours after ingestion of the caustic material. The severity of esophageal injury was classified as follows: grade 0, negative finding; grade 1, injury limited to erythema and edema; grade 2, ulcerations with necrotic tissue and white plaque; and grade 3, injury involving deep ulcerations, white plaque, and necrotic changes.[7] Grade 0 and 1 esophageal injuries were defined as low-grade injuries, while grade 2 and 3 esophageal injuries were defined as high-grade ones. Esophageal stricture was defined as the presence of a constant area of narrowing after contrast swallowing or as stenosis viewed endoscopically.[8] Correlations among signs and symptoms (S/S), inflammatory parameters, the severity of esophageal lesions, and the presence of esophageal stricture were analyzed. We tested the presence of 3 or more signs and symptoms in predicting esophageal injury or stricture because good positive and negative predictive values have been reported.[3,5] Patients with alkali ingestion and potential complications were also analyzed.

The two-tailed Mann-Whitney U test was used to compare the frequency of the S/S in relation to the severity of esophageal injury and stricture. Two-tailed Student t-tests were used to compare leukocyte counts, CRP, and age relative to the range of esophageal injury and stricture. Fisher's exact test was used to test for difference in proportions between patients with and those without esophageal stricture, as well as those with low-grade and high-grade esophageal injury. In multivariate analysis, a forward stepwise logistic regression was performed to assess the set of variables that were independent predictors of esophageal injury or stricture. A p value of less than 0.05 was considered significant; all data are presented as the mean $\pm$ standard error. All statistical analyses were performed using the Statistical Package for the Social Science for Windows (vers. 10.0; SPSS, Chicago, IL, USA).

RESULTS

Of the 32 patients, 16 were boys and 16 girls. Ages ranged from 1.7 to 16.3 (mean, 5.3) years. Twenty-two patients (69%) were below 5 years of age. Alkali agents included lye in 6, sodium hydrate solution or tablets in 3, ammonium bromide in 1, caustic soda in 1, detergent in 6, desiccate in 2, and other materials in 2. Acid agents included hydrochloride in 6, acetic acid in 3, and industrial agents in 2. There were no cases of fatal ingestion in this series.

The CRP was evaluated in 16 patients, and leukocyte counts were checked in all patients. Endoscopy showed negative findings in 6 cases, grade 1 esophageal injury in 10, grade 2 in 12 and grade 3 in 4.

Twenty-two patients presented with less than 3 S/S, while 10 patients had 3 or more. Patients with 3 or more S/S tended to have severe esophageal injury ($p = 0.027$) and esophageal stricture ($p = 0.05$).

In Table 1, the frequency of the S/S of the patients with high-grade injury (mean=2.38) was

higher than that of patients with low-grade injury (mean=1.19) ($p=0.004$). The mean of leukocyte counts of high-grade esophageal injury (16,287.5±1649.4/mm^3) was higher than that of low-grade esophageal injury (12,556.3±1332.3/mm^3); however, it did not reach statistical significance ($p=0.061$). Most patients with low-grade esophageal injury healed without sequelae, except for 1 who developed esophageal stricture. Ten patients with high-grade esophageal injury developed esophageal stricture. Failure of dilatation by bouginage occurred in 6 patients; therefore esophageal reconstructions were performed by colon interposition or ileocolic conduit.

As shown in Table 2, the mean leukocyte count among the 11 patients with stricture (15,136.4±2089.6/mm^3) was similar to that of the 21 patients without esophageal stricture (15,245.5±6344.7/mm^3). Ten of 21 patients with alkali ingestion and 1 of 11 patients with acid ingestion developed esophageal stricture ($p=0.049$). The frequency of the S/S of the patients with stricture (mean=2.73) was higher than that of patients without stricture (mean=1.29) ($p=0.002$).

In patients with alkali ingestion (Table 3), the frequency of S/S of the patients with high-grade injury (mean=2.55) was higher than that of patients with low-grade injury (mean=1.50) ($p=0.032$). The frequency of S/S of patients with stricture (mean=2.80) was higher than that of patients without stricture (mean=1.36) ($p=0.005$). In patients who had ingested alkali, subsequent esophageal stricture was also associated with high-grade esophageal injury ($p=0.002$).

Differences in CRP values as related to the severity of esophageal injury and stricture were also analyzed. There was no statistically significant difference between the 7 patients with high-grade esophageal injury (28.7±17.6 mg/l) and the 9 patients with low-grade injury (21.4±16.6 mg/l) ($p=0.299$). There was also no statistically significant difference between the 5 patients with esophageal stricture (38.6±23.7 mg/l) and the 11 patients without esophageal stricture (27.7±23.3 mg/l) ($p=0.276$).

According to multivariate analysis, vomiting ($p=0.016$) and frequency of S/S ($p=0.011$) were independent factors for a high degree of esophageal injury, while other variables had no statistical significance (Table1). Drooling or dysphagia ($p=0.031$) and frequency of S/S ($p=0.007$) were independent factors for esophageal stricture, while other variables had no statistical significance (Table 2).

Table 1. Data and Prognosis of Patients with Different Degrees of Esophageal Injury

	Severity of esophageal injury, n (%)			Logistic regression
	Low grade N = 16	High grade N = 16	*p*	*p*
Gender (male: female)	7 : 9	9 : 7	0.724	0.541
Age (month)	58.1±15.8	70.1±13.5	0.559	0.892
Caustic agents (alkali: acid)	10: 6	11: 5	1.000	0.811
Fever	3 (19%)	5 (31%)	0.685	0.311
Vomiting	3 (19%)	10 (63%)	0.029	0.016
Oropharyngeal burn	9 (75%)	12 (75%)	0.458	0.284
Drooling or dysphagia	1 (6%)	6 (38%)	0.083	0.052
Abdominal pain or refusal to eat	1 (6%)	3 (19%)	0.600	0.631
Respiratory distress	2 (13%)	2 (13%)	1.000	0.837
Frequency of symptoms and/or signs*	1.19	2.38	0.004	0.011
Leukocyte count (/mm^3)	12556.3±1332.3	16287.5±1649.4	0.061	0.209
Esophageal stricture, n (%)	1 (6.25%)	10 (62.5%)	0.005	
Surgery, n (%)	1 (6.25%)	6 (37.5%)	0.041	
Mortality, n (%)	0 (0%)	0 (0%)		

*The mean frequency of 6 common symptoms and signs of caustic ingestion.
Data are presented as the mean±SE for age and leukocyte count.

Table 2. Demographic and Clinic Data of Patients with or Those without Esophageal Stricture

	Presence of esophageal stricture, n (%)			Logistic regression
	No	Yes	*p*	*p*
	N = 21	N = 11		
Gender (male: female)	10 : 11	6 : 5	1.000	0.829
Age (month)	55.3±17.1	61.3±14.6	0.800	0.600
Caustic agents (alkali: acid)	11 : 10	10 : 1	0.049	0.061
Fever	3 (14%)	5 (45%)	0.088	0.111
Vomiting	6 (29%)	7 (64%)	0.072	0.094
Oropharyngeal burn	12 (57%)	9 (82%)	0.248	0.170
Drooling or dysphagia	2 (10%)	5 (45%)	0.032	0.031
Abdominal pain or refusal to eat	1 (5%)	3 (27%)	0.106	0.053
Respiratory distress	3 (14%)	1 (9%)	1.000	0.592
Frequency of symptoms and/or signs*	1.29	2.73	0.002	0.007
Leukocyte count (/mm^3)	15245.5 ± 6344.7	15136.4 ± 2089.6	0.972	0.975

*The mean frequency of 6 common symptoms and signs of caustic ingestion.
Data are presented as the mean ± SE for age and leukocyte count.

Table 3. Clinical Manifestations and Prognosis in Patients with Ingestion of Alkali

	Esophageal injury, n (%)		*p*	Esophageal stricture, n (%)		*p*
	Low grade	High grade		No	Yes	
	N = 10	N = 11		N = 11	N = 10	
Frequency of symptoms and/or signs*	1.5	2.55	0.032	1.36	2.8	0.005
Esophageal stricture, n (%)	1 (10%)	9 (82%)	0.002			

*The mean frequency of 6 common symptoms and signs of caustic ingestion.

DISCUSSION

Unlike adults, most children swallow caustic materials by accident, and usually they stop as soon as they feel uncomfortable;[9] however, it is almost always too late to avoid resultant esophageal injury.[1] Rapid assessment of the severity of the injury is very important because the prognosis depends on early application of appropriate treatment.[10] Previous studies arrived at different conclusions about the indications for esophagoscopy with ingestion of corrosive materials.[11-13] In 1991, Ashbaugh reported that the risk of instrumental perforation of the esophagus and/or stomach following ingestion was the principal determination for the routine use of early endoscopy.[11] Ciftci, in 1999, reported that the risk of perforation was theoretically much reduced after the introduction of fiberoptic endoscopes.[12] In 1985, Wasserman reported that the presence of significant posterior pharyngeal burns with edema is a contraindication to early esophagoscopy because of the risk of airway obstruction and the necessity of hospitalization for observation.[14] However, some substances like ammonia and bleaches produce marked mucosal edema and rarely penetrate deeply enough to injure the submucosa or muscularis propria.[15] Harley also reported in 1997 that fiberoptic examination of the pharynx and larynx can be safely carried out in such cases.[16] In the current study, we evaluated whether the prognosis was associated with the severity of clinical presentations. If patients presented with more than 3 S/S after ingestion of even a small amount of a caustic material, an endoscopic examination after 12-24 hours appeared helpful and safe for assessing the severity of mucosal inflammation. Patients with a higher degree of esophageal injury had the risk of subsequent esophageal stricture.

In young children, an accurate assessment of the history and symptoms of caustic ingestion is often

difficult. Some studies proposed that initial signs and symptoms were not useful predictors for the severity of esophageal injury and subsequent complications.[3,4] On the other hand, some studies suggested that children with an uncertain history of ingestion and with no symptoms or signs need not be treated.[17] Gaudreault, in 1983, described how outcomes could be predicted based on initial symptoms/signs.[4] In this study, patients with a high degree of esophageal injury or esophageal stricture had a greater number of S/S, especially for those presenting with 3 or more S/S. Therefore, endoscopy for these patients after ingestion of caustic agents is a requisite evaluation modality, and intensive care is necessary.

After ingestion of a caustic material, initial inflammatory changes in the esophagus of erythema, edema, and ulceration appear within the first few days. Formation of granulation tissue and ultimate stricture develop later. The pH, concentration, and duration of contact of the caustic material with the mucosa determine the severity of esophageal injury.[18] Alkali materials tend to injury the esophagus through liquefactive necrosis and penetration, while acid ingestion tends to spare the esophagus because acids rapidly pass through the esophagus with lower degrees of penetration.[12,18] Therefore, alkali ingestion leads to a greater incidence of esophageal stricture than does acid ingestion.

Serum CRP and leukocyte count levels are 2 useful parameters for monitoring inflammation.[19,20] After the onset of acute tissue injury, serum CRP increased within 4 to 6 hours and peaked at 24 to 48 hours.[19] These values are always used in the evaluation of the severity of tissue injury and were found to be proportional to the degree of damage.[21] However, in our cases, leukocyte counts were useful in evaluating the severity of esophageal injury but were not a valuable indicator for esophageal stricture. There was also no statistical significant correlation between CRP and the severity of esophageal injury.

In conclusion, there is an association with a higher degree of esophageal injury and stricture in patients who present with 3 or more of S/S after ingesting caustic agents. The alkali character of caustic materials is associated with esophageal stricture. There is a strong correlation between a higher degree of esophageal injury and subsequent esophageal stricture. For such patients, panendoscopy and intensive follow-up are critical. Serum CRP and leukocyte counts cannot accurately predict the severity of esophageal injury or subsequent esophageal stricture.

REFERENCES

1. Anderson KD, Rouse TM, Randolph JG. A controlled trial of corticosteroids in children with corrosive injury of the esophagus. New Engl J Med 1990;323:637-40.
2. Christesen HB. Epidemiology and prevention of caustic ingestion in children. Acta Paediatr 1994;83:212-5.
3. Christesen HB. Prediction of complications following unintentional caustic ingestion in children. Is endoscopy always necessary? Acta Paediatr 1995;84:1177-82.
4. Gaudreault P, Parent M, McGuigan MA, Chicoine L, Lovejoy FH Jr. Predictability of esophageal injury from signs and symptoms: a study of caustic ingestion in 378 children. Pediatrics 1983;71:767-70.
5. Gorman RL, Khin-Maung-Gyi MT, Klein-Schwartz W, Oderda GM, Benson B, Litovitz T, McCormick M, McElwee N, Spiller H, Krenzelok E. Initial symptoms as predictors of esophageal injury in alkaline corrosive ingestions. Am J Emerg Med 1992;10:189-94.
6. Ferguson MK, Migliore M, Staszak VM, Little AG. Early evaluation and therapy for caustic esophageal injury. Am J Surg 1989;157:116-20.
7. Kirsh MM, Ritter F. Caustic ingestion and subsequent damage to the oropharyngeal and digestive passages. Ann Thorac Surg 1976;21:74-82.
8. Muhletaler CA, Gerlock AJ Jr., de Soto L, Halter SA. Acid corrosive esophagitis: radiographic findings. AJR Am J Roentgenol 1980;134:1137-40.
9. Myers NA. The history of esophageal surgery: pediatric aspects. Pediatr Surg Int 1997;12:101-7.
10. Karjoo M. Caustic ingestion and foreign bodies in the gastrointestinal system. Curr Opin Pediatr 1998;10:516-22.
11. Ashbaugh DG, Jenkins DW, Gainey MD. Gastroscopy in corrosive burn of the stomach. JAMA 1971;216:1638-40.
12. Ciftci AO, Senocak ME, Buyukpamukcu N, Hicsonmez A. Gastric outlet obstruction due to corrosive ingestion: incidence and outcome. Pediatr Surg Int 1999;15:88-91.
13. Zargar SA, Kochhar R, Nagi B, Mehta S, Mehta SK. Ingestion of corrosive acids. Spectrum of injury to upper gastrointestinal tract and natural history. Gastroenterology 1989;97:702-7.
14. Wasserman RL, Ginsburg CM. Caustic substance injuries. J Pediatr 1985;107:169-74.
15. Oakes DD, Sherck JP, Mark JB. Lye ingestion. Clinical patterns and therapeutic implications. J Thorac Cardiovasc Surg 1983;83:194-204.
16. Harley EH, Collins MD. Liquid household bleach ingestion in children: a retrospective review. Laryngoscope

1997;107:122-5.
17. Muhlendahl KE, Oberdisse U, Krienke EG. Local injuries by accidental ingestion of corrosive substances by children. Arch Toxicol 1978;39:299-314.
18. Spitz L. Lakhoo K. Caustic ingestion. Arch Dis Child 1993;68:157-8.
19. Jaye DL, Waites KB. Clinical applications of C-reactive protein in pediatrics. Pediatr Infect Dis J 1997;16:735-47.
20. Shapiro MF, Greenfield S. The complete blood count and leukocyte differential count. An approach to their rational application. Ann Int Med 1987;106:65-74.
21. Pruchniewski D, Pawlowski T, Morkowski J, Mackiewicz S. C-reactive protein in management of children's burns. Ann Clin Res 1987;19:334-8.

兒童意外吞食腐蝕性物質造成食道傷害的預測因子

陳宗義 高常發[1] 莊錦豪[2] 郭馨蔚[3] 刁茂盟

背 景： 臆測吞食腐蝕性物質造成食道傷害的嚴重度對於臨床醫師是一個挑戰性的問題。本研究的目的在探討吞食腐蝕性物質的兒童其臨床表現與預後的相關性。

方 法： 本研究包含了32個食入腐蝕性物質造成食道傷害的兒童。這些病人的徵兆，症狀，白血球數以及C反應蛋白皆有記錄。

結 果： 病人有三種以上之徵兆和症狀者有較爲嚴重的食道傷害及狹窄。嚴重食道受傷的病人比低度受傷的病人有較多的徵兆及症狀。嚴重受傷的病人顯然較爲容易日後發生食道狹窄。食入腐蝕性物質的酸鹼與食道狹窄有關，而與食道受傷程度無關。白血球數與食道受傷嚴重度統計上無顯著差異。在有食道狹窄病人的白血球數平均值接近於無食道狹窄病人的白血球平均值。C反應蛋白在兩組病人之間統計上亦無顯著差異。

結 論： 基於以上的資料，對於預測食道腐蝕性傷害後，食道受傷及嚴重度而言，白血球及C反應蛋白不是有用的指標。吞食鹼性物質比酸性物質更可能發生食道狹窄。吞食腐蝕性物質後，愈多的徵兆需要愈積極的處置。

(長庚醫誌 2003;26:233-9)

關鍵字： 白血球，C反應蛋白，腐蝕性，食道，狹窄。

長庚兒童醫院 高雄院區 兒童內科，[1]放射診斷科，[2]兒童外科，[3]高雄醫學大學 內科
受文日期：民國91年9月17日；接受刊載：民國92年1月9日。
索取抽印本處：刁茂盟醫師，長庚紀念醫院 兒童內科。高雄縣833鳥松鄉大埤路123號。Tel: (07)7317123; Fax: (07)7338009; E-mail: tsungyi@ms30.url.com.tw