Observational Study

Medicine®

OPEN

Endoscopic findings and outcome in caustic ingestion of acidic and alkaline agents in adults

A retrospective analysis

Marcus Hollenbach, MD[a,*], Jan Tünnemann, MD[a], Manuel Florian Struck, MD[b], Jürgen Feisthammel, MD[a], Tobias Schlosser, MD[a], Tiffany Schaumburg[a], Joachim Mössner, MD, PhD[a], Albrecht Hoffmeister, MD, PhD[a]

Abstract

Caustic ingestion in adults is a rare but potentially life-threatening problem. It remains controversial whether endoscopic findings and mortality differ between acid and alkali ingestion. We compared ingestion of these agents and evaluated prediction parameters for survival and complications.

Adult patients who presented with caustic ingestion were analyzed from 2005 to 2016. Mucosal injury was graded endoscopically by Zargar's score. Age, gender, intent of ingestion, caustic agents, comorbidities, management, complications, and mortality were examined.

Thirty-one patients met inclusion criteria and were divided into acid (n = 10) and alkali group (n = 21). Ingestion of alkali resulted in higher grades (≥III) of esophageal (56% vs 24%, $P = .01$) and stomach injuries (43% vs 13%, $P = .05$) and was mostly done with suicidal intent (76% vs 30%, $P = .003$). Patients in the alkali group received more often surgical interventions, mechanical ventilation and tracheotomy. Overall complications including Zargar's-score ≥ grade III, mediastinitis, and aspiration pneumonia were higher in alkali group but all showed no statistical significance ($P = .73$). Mortality (acid: 1 (10%), alkali: 4 (19%), $P = .52$), age, gender, comorbidities, and intensive care management did not differ significantly between the groups. Chronic renal failure and mediastinitis were promising prediction parameters for mortality but did not reach statistical significance. No independent risk factors for the development of esophageal stenosis were identified.

Alkaline agents caused a higher mucosal injury severity and were more often used in suicidal intent. Mediastinitis and chronic renal failure might be potential prediction parameters for survival but need to be evaluated in larger studies.

Abbreviations: CI = confidence interval, COPD = chronic obstructive pulmonary disease, CT = computed tomography, CXR = chest radiography, ED = emergency department, ER = emergency room, ICD 10 = international classification of diseases revision 10, ICU = intensive care unit, OR = odds ratio, S.D. = standard deviation.

Keywords: acid, alkali, endoscopy, ingestion, zargar score

1. Introduction

The ingestion of caustic substances into the upper gastrointestinal tract in adults is an unusual but potentially life-threatening problem.[1] Incidence varies with regard to national and cultural background between 5,000 and 15,000 cases annually.[2] In contrast to mostly accidental ingestion in children,[3] the ingestion of corrosive solutions in adults is predominantly performed with suicidal intent or due to psychiatric disorders.[4]

The severity of tissue lesions caused by corrosive substances depends on type, quantity, concentration, and contact time. The prevalence of esophageal pathologies also may influence the severity of mucosal damage.[5,6] Acids usually cause coagulation necrosis with denaturation of superficial proteins and formation of eschar. Although eschar may prevent from further tissue damage, it may also work destructively by leading to obstruction and increasing the risk of perforation or bleeding.[7] In contrast, alkaline solutions may lead to liquefactive necrosis and subsequent deep tissue injuries, depending on the exposure time. Prolonged contact with alkaline substances also increases the risk of stricture formation.[8]

The majority of studies analyzing outcome and management of caustic ingestion were performed in children and only a few surveys with different study design described caustic ingestion in adults.[9–19] Moreover, mostly techniques and complications of surgical procedures after ingestion of corrosive agents were analyzed.[20,21] Thus, the aim of the present study was to evaluate both endoscopic findings and outcome after ingestion of different corrosive agents in adults. We analyzed the Zargar severity

Editor: Sherief Abd-Elsalam.

MH and JT contributed equally to this work.

We acknowledge support from the German Research Foundation (DFG) and the University of Leipzig within the program of Open Access Publishing (to MH).

The authors have no conflicts of interest to declare.

[a] Medical Department II – Gastroenterology, Hepatology, Infectious Diseases, Pulmonology, [b] Department of Anaesthesiology and Intensive Care Medicine, University of Leipzig Medical Center, Leipzig, Germany.

[*] Correspondence: Marcus Hollenbach, Medical Department II - Gastroenterology, Hepatology, Infectious Diseases, Pulmonology, University of Leipzig Medical Center, Liebigstrasse 20, D-04103 Leipzig, Germany (e-mail: marcus.hollenbach@medizin.uni-leipzig.de).

Medicine (2019) 98:35(e16729)

Received: 21 December 2018 / Received in final form: 26 June 2019 / Accepted: 13 July 2019

http://dx.doi.org/10.1097/MD.0000000000016729

score[22] and compared complications and management between acid or alkali ingestion. Potential risk factors for development of esophageal stenosis and prediction parameters for survival were identified by means of logistic regression analysis.

2. Patients and methods

2.1. Patient selection

After approval of the ethics committee of the Medical faculty of the University of Leipzig (No. 137–15–20042015), we retrospectively evaluated the data of adult patients with caustic ingestion who had been treated in our university hospital between January 2005 and December 2016. The medical database was reviewed to identify patients classified by the ICD-10 system for caustic injury and chemical burn (ICD-10 code T27.x and T28.x). If performed, standard endoscopes (9.6 mm or less in diameter) were used under minimal air insufflation for endoscopic examination of the upper gastrointestinal tract. Extreme care was used passing injured sections of the esophagus, stomach, or duodenum. All endoscopic procedures were performed by experienced endoscopists.

2.2. Parameters

Subjects were divided into 2 groups: ingestion of either acidic or alkaline caustic agents. The type of caustic agent ingested and, if specified, the approximate volumes were registered. Medical records were evaluated for patient demographics including age, gender, intent of ingestion, corrosive agent, quantity, and co-intoxications. Reports were analyzed further for comorbidities, for example, congestive heart failure, arterial hypertension, diabetes, chronic renal failure, chronic obstructive pulmonary disease (COPD), malignant diseases, neurologic, and psychiatric disorders.

Mucosal injuries of the esophagus, stomach and duodenum were retrospectively graded according to the modified endoscopic classification of Zargar et al [22]: grade 0 = no mucosal damage, grade I = edema and hyperemia; grade IIa = superficial ulceration, erosions, friability, blisters, exudates, hemorrhages, or whitish membranes; grade IIb = additional deep, discrete, or circumferential ulcerations; grade IIIa = small scattered areas of multiple ulcerations and areas of necrosis with brown-black or grayish discoloration; grade IIIb = extensive necrosis; grade IV = perforation. Perforation was diagnosed by the presence of free air on a plain chest radiograph, computes tomography (CT) scan or by endoscopy. Representative endoscopic images are shown in Figure 1.

Procedural data was also assessed, which comprised necessity for intensive care unit (ICU) admission, tracheotomy, nasojejunal probe, CT scan, antibiotic therapy, and surgical intervention. Clinical outcome was assessed by determination of esophageal stenosis in follow-up endoscopy, development of mediastinitis, aspiration pneumonia, pharyngeal involvement (edema, erosion, or ulcera), length of hospital stay, and mortality. Esophageal stricture was diagnosed by endoscopy or defined as dysphagia, symptoms of regurgitation or difficulty of swallowing as indicated by patient complaints.

2.3. Patient management

All patients admitted to the hospital were examined and stratified for further therapy in our emergency department (ED). Blood tests, including complete blood and differential counts, and measurements of transaminases, creatinine, electrolytes, and inflammation markers were performed in the ED. Based on the interdisciplinary judgement of emergency physicians, intensivists, gastroenterologists, and surgeons, patients were admitted either to the ICU or the normal ward and endoscopy was performed unless otherwise indicated. All patients were treated with proton pump inhibitors. Oral intake was withheld, and parenteral or enteral nutrition by nasojejunal tube was provided until perforation or severe mucosal damage was excluded and the condition of the patient had stabilized. Antibiotics were administered depending on the supervising clinician's judgement. Aspiration pneumonia was diagnosed by chest radiography (CXR) or CT scan. Overall, the diagnostic and therapeutic procedures were discussed interdisciplinary and performed as a result of physician's decision.

Surviving patients were followed at the outpatient clinic for at least 1 month. Seven patients signed themselves out against medical advice and were lost for follow-up. If symptoms of dysphagia occurred during follow-up, an endoscopy was performed for the evaluation of an esophageal stricture.

2.4. Statistical analyses

Demographic, endoscopic, clinical, and procedural findings are presented as "n" with a percentage (%) to each corresponding group. Exceptions are made in the parameters age, length of hospital stay and volume of ingested agent, which are expressed as a mean with standard deviation (S.D.). Student t test was applied to analyze dispersions in age and ingested volume after passing normality distribution by D'Agostino and Pearsons omnibus normality test. Mann–Whitney U test was used to analyze days to endoscopy and length of hospital stay which were not normally distributed.

Chi-square or Fisher exact tests were performed to identify dispersions in patient characteristics, endoscopic findings and clinical findings among the acid and alkali ingestion group. Survival was examined by Kaplan–Meier analysis with a log-rank test to indicate the cumulative survival rate pertaining to acid or alkali ingestion. To identify risk factors for survival or the development of an esophageal stricture, univariate logistic regression models were performed to obtain the proportional odds ratio (OR) with a 95% confidence interval. Statistical assessments were considered to be significant at a P value of less than .05 except regression analysis. The level of significance in univariate analysis was set to .005 due to testing of multiple parameters. Statistical analyses were performed by means of GraphPad Prism 4.0 (La Jolla, USA) and XLSTAT (Addinsoft, STATCON, Witzenhausen, Germany).

3. Results

3.1. Patient characteristics

We retrospectively identified 31 adult patients admitted to the hospital with caustic ingestion of the upper gastrointestinal tract. In the acid ingestion group, 10 patients mainly ingested vinegar or a purely acidic substance. The ingestion of the acidic agents was predominantly accidental (70%), and only a small minority of the patients had a suicidal intent (30%). In the alkali group, 21 patients ingested cleaning agents and laundry detergents, and in most cases did so with a suicidal intent (76%). Statistical analysis of the intent of ingestion and the ingested agents was significantly different between both groups ($P = .003$ and $P < .001$). In

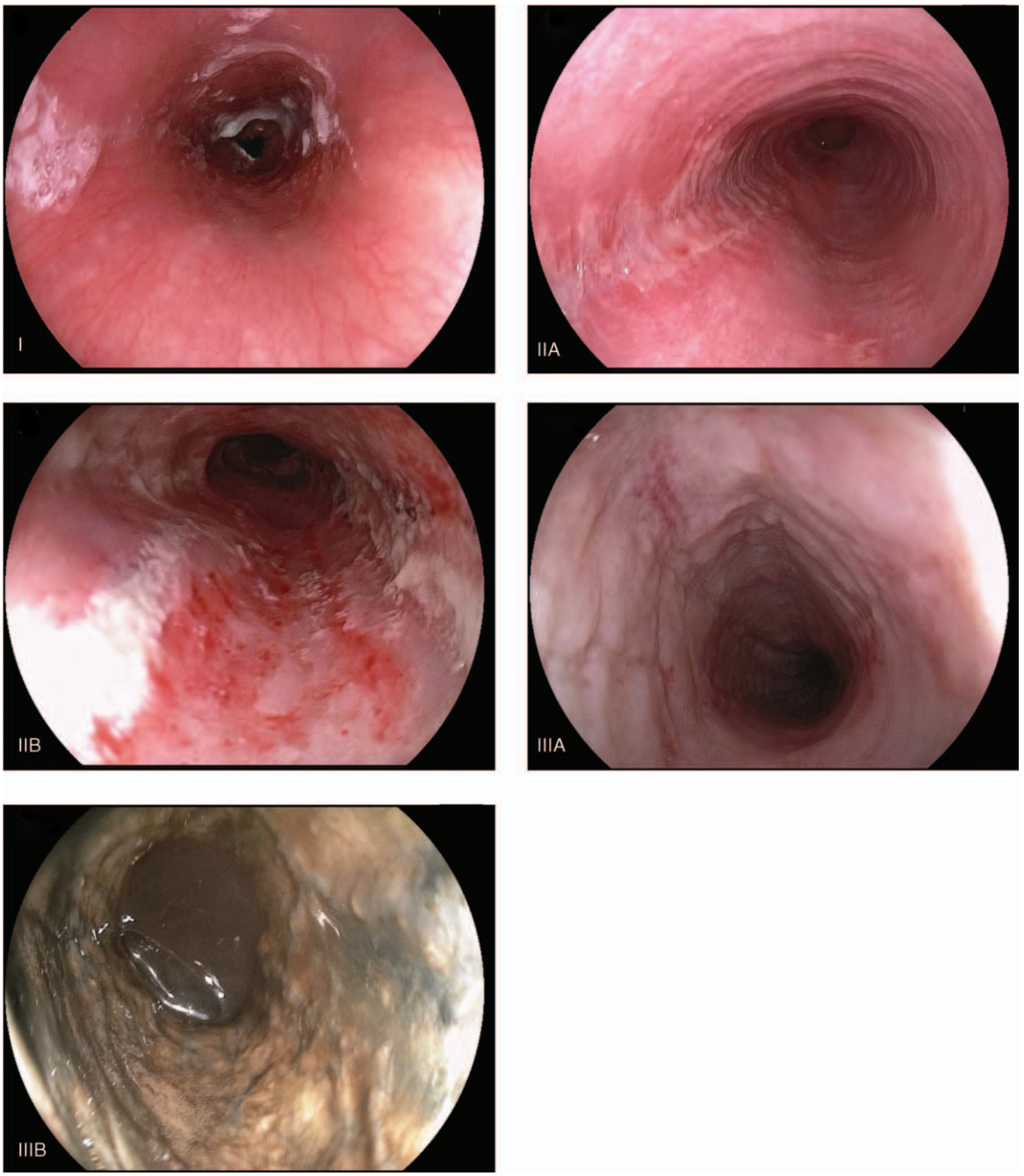

Figure 1. Endoscopic findings after caustic ingestion related to Zargar score.

contrast, age (54 ± 22y vs 45 ± 19y, $P = .24$), female gender (60% vs 33%, $P = .25$), volume of the ingested agent (159 ± 162 ml vs 278 ± 225 ml, $P = .22$) and co-intoxications (10% vs 38%, $P = .75$) did not differ significantly between the acid and alkali groups (see Table 1). Moreover, no significant differences in co-intoxication were registered when comparing patients with suicidal (32%) or accidental (25%, $P = .69$, data not shown) ingestion of corrosive agents.

To determine risk factors for the outcome of caustic ingestion, we analyzed patients' comorbidities. Statistical analysis of the acid and alkali groups revealed no significant differences in the presence of congestive heart failure (10% vs 14%, $P = .74$), arterial hypertension (20% vs 19%, $P = .95$), diabetes (20% vs 13%, $P = .69$), chronic renal failure (10% vs 10%, $P = .96$), COPD (10% vs 5%, $P = .58$), malignant diseases (0% vs 10%, $P = .31$), neurologic (0% vs 10%, $P = .31$) or psychiatric disorders (40% vs 33%, $P = .72$; see Table 2).

3.2. Endoscopic findings

In eight of the acid group patients (80%) and 16 of the alkali group patients (76%), endoscopy was performed in order to evaluate the severity of the mucosal injury. Analysis indicated significantly more high-grade (according to Zargar's score)

Table 1

Characteristics of 31 adults referred for caustic ingestion.

	Acid	Alkali	*P*
Number of patients (%)	10	21	
Age (years)	54 ± 22	45 ± 19	.24
Female gender (%)	6 (60)	7 (33)	.25
Intent of ingestion (%)			**.003**
Accident	7 (70)	5 (24)	
Suicide	3 (30)	16 (76)	
Caustic products (%)			**<.001**
Strong acid	3 (30)	0 (0)	
Strong soda	0 (0)	1 (5)	
Cleaning agent	1 (10)	13 (62)	
Laundry detergent	0 (0)	5 (24)	
Oven cleaner	0 (0)	1 (5)	
Vinegar	4 (40)	0 (0)	
Fertilizer	1 (10)	0 (0)	
Others	1 (10)	1 (5)	
Mean quantity of ingested agent (ml)	159 ± 162	278 ± 225	.22
Co-intoxications (%)			.75
all	1 (10)	8 (38)	
alcohol	1 (10)	5 (24)	
opiates	0 (10)	0 (0)	
tranquillizers	0 (0)	1 (5)	
others	0 (0)	2 (10)	

Analysis by student *t* test, Fisher exact test and Chi-square test. Statistical significance: $P < .05$.

lesions in the esophagus (≥ grade III: 56% vs 24%, $P = .01$) and in the stomach (≥ grade III: 43% vs 13%, $P = .05$) in the alkali group. The severity of the mucosal lesions in the duodenum, however, did not differ significantly between both groups (≥ grade III: 6% vs 0%, $P = .09$; see Table 3). Perforation was diagnosed in only 1 patient in the alkali group (none in the acid group). No iatrogenic perforations occurred during endoscopic examinations. Representative endoscopic images of different grades of mucosal injury can be found in Figure 1.

3.3. Clinical data and outcome

In the acid ingestion group, 60% of patients were admitted to ICU compared to 81% in the alkali ingestion group ($P = .38$). In both groups, a comparable number of patients underwent CT scan (20% vs 30%, $P = .24$) and antibiotic therapy (40% vs 52%, $P = .70$). Patients received more often invasive ventilation with endotracheal intubation (57% vs 30%, $P = .25$), tracheotomy (33% vs 0%, $P = .15$) and follow-up endoscopy (67% vs 40%, $P = .25$) after ingestion of alkaline agents, but these differences remained insignificant. Surgical intervention was necessary only in the alkali ingestion group (24% vs 0%, $P = .15$). Hereby, 4 patients received emergency resection of the esophagus within 48 hours (1 patient with esophagogastric anastomosis and 3 with esophagojejunal anastomosis). Additionally, 1 patient received delayed esophagectomy with colon interposition after more than 3 months. In contrast, significantly more patients were fed through nasojejunal tubes (38% vs 0%, $P = .03$) after the ingestion of alkaline agents and received earlier endoscopic evaluation (0.68d vs 1.75d after ingestion, $P = .03$; see Table 4).

Table 2

Comorbidities of patients.

	Acid	Alkali	*P*
Congestive heart failure (%)	1 (10)	3 (14)	.74
Arterial hypertension (%)	2 (20)	4 (19)	.95
Diabetes (%)	2 (20)	3 (13)	.69
Chronic renal failure (%)	1 (10)	2 (10)	.96
COPD (%)	1 (10)	1 (5)	.58
Malignant diseases (%)	0 (0)	2 (10)	.31
Neurologic disorders (%)	0 (0)	2 (10)	.31
Psychiatric disorders (%)	4 (40)	7 (33)	.72

Analysis by Fisher exact test and Chi-square test. Statistical significance: $P < .05$. COPD = chronic obstructive pulmonary disease.

Table 3

Endoscopic findings according to Zargar classification.

	Acid	Alkali	*P*
Initial endoscopy (%)	8/10 (80)	16/21 (76)	>.99
Esophagus			**.01**
Grade 0 (normal)	0 (0)	1 (6)	
Grade I (hyperemia, edema)	3 (38)	1 (6)	
Grade IIa (spf. ulcerations)	3 (38)	3 (19)	
Grade IIb (deep ulcerations)	0 (0)	2 (13)	
Grade IIIa (less necrosis)	2 (24)	1 (6)	
Grade IIIb (extensive necr.)	0 (0)	7 (44)	
Grade IV (perforation)	0 (0)	1 (6)	
Stomach			**.04**
Grade 0	0 (0)	2 (13)	
Grade I	5 (62)	1 (6)	
Grade IIa	2 (25)	2 (13)	
Grade IIb	0 (0)	4 (25)	
Grade IIIa	1 (13)	6 (37)	
Grade IIIb	0 (0)	1 (6)	
Grade IV	0 (0)	0 (0)	
Duodenum			.09
Grade 0	6 (74)	7 (42)	
Grade I	1 (13)	2 (14)	
Grade IIa	1 (13)	4 (25)	
Grade IIb	0 (0)	2 (13)	
Grade IIIa	0 (0)	1 (6)	
Grade IIIb	0 (0)	0 (0)	
Grade IV	0 (0)	0 (0)	

Analysis by Fisher exact test and Chi-square test. Statistical significance: $P < .05$.

Table 4

Procedural data and outcome.

	Acid	Alkali	*P*
Admission to ICU (%)	6 (60)	17 (81)	.38
Tracheotomy (%)	0 (0)	7 (33)	.07
Nasojejunal probe (%)	0 (0)	8 (38)	.03
Endotracheal intubation (%)	3 (30)	12 (57)	.25
Initial CT scan (%)	2 (20)	10 (30)	.24
Surgery (%)	0 (0)	5 (24)	.14
Initial (within 48 hours)	0	4	
Delayed (> 4 weeks)	0	1	
Days to initial endoscopy (mean)	1.75	0.68	.03
Follow-up endoscopy (%)	4 (40)	14 (67)	.25
Antibiotic therapy (%)	4 (40)	11 (52)	.70
Esophageal stenosis (%)	1 (10)	4 (19)	.52
Mediastinitis (%)	0 (0)	4 (19)	.15
Aspiration pneumoniae (%)	0 (0)	3 (14)	.53
Pharyngeal involvement (%)	3 (30)	8 (38)	.66
Lenght of hospital stay (d)	10.9 ± 9.2	21.1 ± 22.9	.30
Mortality (%)	1 (10)	4 (19)	.52

Analysis by student *t* test, Fisher exact test and Chi-square test. Statistical significance: $P < .05$. ICU = intensive care unit, CT = computer tomography.

Next, we analyzed the severity after ingestion of alkaline or acidic agents. Our data showed higher rate of complications, such as occurrence of esophageal stenosis (alkali group: 19%, acid group: 10%, $P=.52$), mediastinitis (alkali group: 19%, acid group: 0%, $P=.15$), aspiration pneumonia (alkali group: 14%, acid group: 0%, $P=.53$), pharyngeal involvement (alkali group: 38%, acid group: 30%, $P=.66$) and the length of the hospital stay (alkali group: 21.1 ± 22.9d, acid group: 10.9 ± 9.2d, $P=.30$) in the alkali group. Nevertheless, these differences showed no statistical significance. Thus, we performed a combined analysis of initial complications including Zargar-score ≥ grade III, mediastinitis, aspiration pneumonia and pharyngeal involvement. However, the rate of overall complications did not differ significantly between both groups ($P=.73$). Although mortality was higher after the ingestion of alkaline agents (4 patients, 19%) compared to that of acidic agents (1 patient, 10%), this difference remained statistically insignificant ($P=.52$; see Table 4). These patients mainly deceased from multi organ failure and sepsis within 18.6 ± 17.5d. Surgery was evaluated in these patients but was not considered as therapeutic option.

3.4. Predictors for survival and esophageal stenosis

We aimed to identify predictors for overall survival as well as the potential development of an esophageal stenosis. In univariate logistic regression analysis, we found no statistically significant predictors for survival. Although chronic renal failure (OR = 16.67, CI = 1.14–243.72, $P=.04$) and mediastinitis (OR = 18.0, CI = 1.81–179.22, $P=.01$) were promising, they did not reach the adjusted level of significance in multiple testing ($P<.005$). Also, age, female gender, suicidal intent, ingestion of alkaline agents, psychiatric disorder, ≥ grade III injury of the esophagus, stomach, or duodenum showed no statistically significant correlation with survival (see Table 5).

Univariate logistic regression analysis for the development of esophageal stenosis could not identify any significant predictors. The OR and CI for age, female gender, suicidal intent, alkali ingestion, psychiatric disorders, chronic renal failure, mediastinitis, ≥ grade III injury of the esophagus, stomach, and duodenum also were no predictors for esophageal stenosis (see Table 6). Multivariate analysis for development of esophageal stenosis or mortality was not able to identify prediction parameters (data not shown).

In addition, the Kaplan–Meier survival curves and log rank test revealed no significant differences in either group regarding patients' survival ($P=.86$; data not shown). The average follow-up time was 133.2 weeks.

Table 5

Univariate regression analysis for mortality.

Parameter	OR	Univariate 95% CI	P
Age	1.03	(0.99–1.08)	.17
Female gender	0.91	(0.13–6.40)	.92
Suicidal intent	1.07	(0.15–7.54)	.95
Alkaline ingestion	2.12	(0.21–21.89)	.53
Psychiatric disorder	3.38	(0.47–24.29)	.23
Chronic renal failure	16.67	(1.14–243.72)	.04
Mediastinitis	18.00	(1.81–179.22)	.01
Grade of esophag. injury ≥ III	4.50	(0.40–51.30)	.23
Grade of stomach injury ≥ III	2.33	(0.26–20.66)	.45
Grade of duodenal injury ≥ III	1.44	(0.01–150.45)	.88

Statistical significance: $P<.005$. OR = odds ratio.

Table 6

Univariate regression analysis for esophageal stenosis.

Parameter	OR	Univariate 95% CI	P
Age	0.96	(0.89–1.03)	.22
Female gender	0.40	(0.03–4.68)	.47
Suicidal intent	3.38	(0.40–28.75)	.27
Alkaline ingestion	1.20	(0.09–15.26)	.89
Psychiatric disorder	0.78	(0.10–6.32)	.81
Chronic renal failure	0.39	(−1.99–0.08)	.07
Mediastinitis	0.14	(0.01–4.05)	.25
Grade of esophag. injury ≥ III	0.42	(0.05–3.44)	.42
Grade of stomach injury ≥ III	0.78	(0.10–6.32)	.81
Grade of duodenal injury ≥ III	0.75	(0.01–78.64)	.91

Statistical significance: $P<.005$. OR = odds ratio.

4. Discussion

Caustic ingestion in adults is a rare but potentially life-threatening problem. Several diagnostic and therapeutic recommendations have been implicated over the last years.[23,24] Nevertheless, a comparison of acidic and alkaline agent ingestion in adults with regard to clinical management, outcome, and survival has not been performed. With this in mind, we retrospectively analyzed all adults with caustic ingestion in our tertiary medical center from 2005 to 2016. We consecutively identified 31 patients (10 with acidic agents and 21 with alkaline agents). Ingestion of alkaline agents was more frequent and revealed higher grades of mucosal injury to the esophagus and stomach along with a heightened suicidal intent. Patients in the alkali group received more often surgical interventions, mechanical ventilation, and tracheotomy without significant differences. Mortality and gastrointestinal complications were higher after ingestion of alkali but no statistical significance was observed. Mediastinitis and chronic renal failure were promising parameters in regression analysis but failed the level of significance. The Zargar's score for mucosal injury did not correlate with patients' outcome. In addition, regression analysis failed to reveal risk factors for the development of esophageal strictures.

Studies analyzing caustic ingestion in adults with regard to survival, clinical outcome and esophageal stenosis remain heterogeneous.[9–19] In these cohorts (see also Table 7), mostly patients with Asian ethnicity were analyzed contrary to the Caucasian ethnic background in our cohort. Hence, the different types of household cleaning products, that are used in Asia[25,26] and Europe,[27] could influence the grade of mucosal injuries after ingestion.

Previous publications identified age, sex, suicidal intent, quantity, time of exposure, and endoscopic grading as prediction markers for severe injuries but did not analyze the risk factors for mortality or esophageal strictures, as was our aim in this study.[28] Moreover, Cheng et al found no differences in grade of mucosal injury between ingestion of acidic of alkaline agents.[11] In contrast, our data clearly showed more extensive mucosal injury after ingestion of alkaline compared to acidic agents. These differences could be explained by the fact that the authors did not differentiate between esophageal and gastric injuries, or that the ingested volume was lower in all patients (approx. < 100 ml) in this study compared to our data. Nevertheless, current data, that

Table 7

Selected cohort studies of outcome of caustic ingestion in adults.

Study	n	Age (y)	% male	Suicide intent (%)	Mortality (%)	Stenosis (%)
Cabral 2012[7]	315	40	43.8	75.9	7	NA
Chang 2011[8]	389	43.25	48.6	72.5	6.2	20.8
Cheng 2008[9]	273	43.77	46.52	71.04	6.59	24.18
Chirica 2016[10]	197	44	55	96	19.6	46.3
Chou 2010[11]	71	54.7	49	NA	42.3	NA
Kochhar 2009[12]	94	29.3	41.48	NA	NA	59.57
Kochhar 2017[13]	62	33	56.45	NA	NA	46.77
Lu 2014[14]	108	50.1	45.37	NA	9.3	43.51
Tohda 2008[15]	95	37.2	61	49	1.1	NA
Zhang 2013[16]	13	30.69	53.84	NA	0	13
Zerbib 2011[17]	70	48	46	90	5.7	34.8
This study	31	48	58.06	61.29	16.13	16.13

identified the grade of mucosal injury as main factor determining outcome,[9] further support our findings. Similarly, recent studies identified patient age >65 years as an important risk factor for morbidity and mortality in caustic ingestion. Additional important predictors for survival were aspiration pneumonia, elevated liver values, systemic complications, and grade of mucosal injury.[10,13] In contrast to these findings, we could not identify the above mentioned parameters as independent risk factors for either survival or esophageal strictures in our patient cohort, which may have several explanations. First, our patients were younger in age (54 ± 22 years in the acid group and 45 ± 19 years in the alkali group). Only 7 patients were older than 65 years, so this subpopulation may be too small to affect statistical results. Furthermore, the absent correlation of grade of mucosal injury with survival or development of esophageal stenosis could be a result of the relatively low number of analyzed patients.

Our results suggest that alkaline agents are used more often than acidic substances in caustic ingestion with suicidal intent. Alkali ingestion is also accompanied with more severe lesions of the esophagus and stomach. This could be explained by the fact, that typical household cleaning goods mostly contain alkaline agents (e.g. cleaning agents and laundry detergents) and are therefore widely available. Another interpretation of our results could be that patients ingest more volume in a suicidal attempt than patients who accidentally intake these liquids. So, one could suggest that the suicidal intent was the reason for more severe mucosal damage in the alkali group and not the agent. However, several findings rebut this theory. First, co-intoxications, that could influence the severe of mucosal damage, were in the alkali group not statistically significant higher and mainly alcohol was used. So, it is unlikely that co-intoxications affected the outcome in the alkali group. Furthermore, comorbidities and other baseline characteristics did not differ between both groups and did not contribute to the suicidal intent. Also, an important argument is that the ingested volume showed a trend to be higher in the alkali group but this trend remained statistically insignificant. In addition, suicidal intent could not be identified as independent risk factor for survival or esophageal stenosis in our study. Thus, suicidal intent *alone* is an unlikely explanation for the more severe mucosal damage in the alkali group.

Our results are strengthened by recent work analyzing caustic agents in development of esophageal stenosis or gastric outlet obstruction.[16] The authors found no differences between acid and alkali ingestion in development of esophageal strictures. Neither age nor gender could be identified as independent risk factors for esophageal strictures. In addition, univariate and multivariate analysis failed to show an association of gender, type of ingested agent or the grade of mucosal injury with mortality in this study, as it was demonstrated in our cohort.

Other studies, however, showed that a preingestion of acidic agents was more likely to affect the stomach than alkaline substances.[29,30] Previous work also showed that the relative extent of esophageal and gastric involvement largely depends on the nature and volume of the corrosive ingested.[31] Alkaline substances are known to be more viscous and can thereby cause liquefaction necrosis by adhering to the esophageal wall. Thus, only a relatively small amount will ever theoretically reach the stomach.[21] However, after the ingestion of a large volume of an alkaline agent, the stomach mucosa will also incur injury. In addition, the mucosal barrier of the stomach protects against acidic substances but not in case of ingestion of alkaline agents. In our study, the alkali group showed a trend toward larger volumes of ingested agents (278 ml) compared to the acid group (159 ml, without statistical significance). The larger volume of ingested alkali could be an explanation for the higher grade of mucosal damage in both esophagus and stomach. However, the evaluation of the volumes of the ingested agents was performed retrospectively from patient files and patient statements. A statistical bias due to inaccurate information could not be excluded.

In addition, we identified only 1 perforation in index endoscopy in the alkali group. No iatrogenic perforations occurred during endoscopic examinations, although this complication is mentioned in the literature.[32] This finding might be explained by the careful examination with small diameter endoscopes.[33] On the other hand, we could not exclude a statistical bias due to already mentioned low patient number. Furthermore, a recent study demonstrated that relook endoscopy after 5 days predicts development of esophageal stenosis more accurate than immediate endoscopy.[15] In our study and the majority of the studies analyzing caustic ingestion, immediate endoscopy was performed. Thus, delayed endoscopy could help to identify predictions parameters of esophageal stenosis after caustic ingestion in future studies. Also, the above-mentioned studies support the clinical practice of careful endoscopic examination with small diameter endoscopes in caustic ingestion without increasing the risk of perforation. A short overview of outcome of the most important cohort studies investigating caustic ingestion in adults can be found in Table 7.

Our study has some limitations. As mentioned above, the number of patients analyzed in this study was relatively small.

Thus, the loss of prediction parameters in regression analysis might be a result of underpowered statistics. Also, surgical interventions, mediastinitis, mechanical ventilation, tracheotomy, complication rates, and mortality were higher after ingestion of alkaline agents but were of no statistical significance. Similarly, we could not identify a higher grade of mucosal injury as prediction parameter for survival or esophageal stenosis, although the ingestion of alkaline agents resulted in significantly more severe mucosal injuries. Therefore, our study might be underpowered due to low number of patients. Furthermore, our study is a retrospective study and the follow-up time may be too short for the evaluation of long-term complications, such as malignant diseases. Nevertheless, our work revealed several interesting findings and may contribute to mucosal injury due to caustic ingestion in adults.

5. Conclusions

In conclusion, our study demonstrated higher grades of tissue damage after caustic ingestion of alkaline compared to acidic agents, mostly in patients with suicidal intent. Grade of mucosal injury, or rate of complications did not predict mortality or esophageal stenosis whereas mediastinitis and chronic renal failure might serve as prognostic parameters for survival and should be subject of future studies.

Author contributions

Conceptualization: Marcus Hollenbach, Albrecht Hoffmeister.
Data curation: Jan Tünnemann, Manuel Florian Struck.
Formal analysis: Marcus Hollenbach.
Funding acquisition: Marcus Hollenbach.
Investigation: Marcus Hollenbach, Jan Tünnemann, Manuel Florian Struck.
Methodology: Jan Tünnemann.
Project administration: Marcus Hollenbach, Albrecht Hoffmeister.
Resources: Manuel Florian Struck, Albrecht Hoffmeister.
Software: Marcus Hollenbach, Manuel Florian Struck.
Supervision: Jürgen Feisthammel, Joachim Mössner, Albrecht Hoffmeister.
Validation: Jürgen Feisthammel, Tobias Schlosser, Tiffany Schaumburg, Albrecht Hoffmeister.
Visualization: Marcus Hollenbach.
Writing – original draft: Marcus Hollenbach.
Writing – review & editing: Jan Tünnemann, Manuel Florian Struck, Jürgen Feisthammel, Tobias Schlosser, Tiffany Schaumburg, Joachim Mössner, Albrecht Hoffmeister.
Marcus Hollenbach orcid: 0000-0002-2654-3164.

References

[1] Chirica M, Bonavina L, Kelly MD, et al. Caustic ingestion. Lancet 2017;389:2041–52.
[2] Schaffer SB, Hebert AF. Caustic ingestion. J La State Med Soc 2000;152:590–6.
[3] Kay M, Wyllie R. Caustic ingestions in children. Curr Opin Pediatr 2009;21:651–4.
[4] Mamede RC, de Mello Filho FV. Ingestion of caustic substances and its complications. Sao Paulo Med J 2001;119:10–5.
[5] Zhang ZL, Wang JL, Guo CL, et al. Ectopic liver tissue in the esophagus: a case report. Medicine (Baltimore) 2019;98:e15260.
[6] Lupu VV, Ignat A, Paduraru G, et al. Heterotopic gastric mucosa in the distal part of esophagus in a teenager: case report. Medicine (Baltimore) 2015;94:e1722.
[7] Espinola TE, Amedee RG. Caustic ingestion and esophageal injury. J La State Med Soc 1993;145:121–5.
[8] Contini S, Scarpignato C. Caustic injury of the upper gastrointestinal tract: a comprehensive review. World J Gastroenterol 2013;19:3918–30.
[9] Cabral C, Chirica M, de CC, et al. Caustic injuries of the upper digestive tract: a population observational study. Surg Endosc 2012;26:214–21.
[10] Chang JM, Liu NJ, Pai BC, et al. The role of age in predicting the outcome of caustic ingestion in adults: a retrospective analysis. BMC Gastroenterol 2011;11:72.
[11] Cheng HT, Cheng CL, Lin CH, et al. Caustic ingestion in adults: the role of endoscopic classification in predicting outcome. BMC Gastroenterol 2008;8:31.
[12] Chirica M, Resche-Rigon M, Zagdanski AM, et al. Computed tomography evaluation of esophagogastric necrosis after caustic ingestion. Ann Surg 2016;264:107–13.
[13] Chou SH, Chang YT, Li HP, et al. Factors predicting the hospital mortality of patients with corrosive gastrointestinal injuries receiving esophagogastrectomy in the acute stage. World J Surg 2010;34:2383–8.
[14] Kochhar R, Poornachandra KS, Puri P, et al. Comparative evaluation of nasoenteral feeding and jejunostomy feeding in acute corrosive injury: a retrospective analysis. Gastrointest Endosc 2009;70:874–80.
[15] Kochhar R, Ashat M, Reddy YR, et al. Relook endoscopy predicts the development of esophageal and antropyloric stenosis better than immediate endoscopy in patients with caustic ingestion. Endoscopy 2017;49:643–50.
[16] Lu LS, Tai WC, Hu ML, et al. Predicting the progress of caustic injury to complicated gastric outlet obstruction and esophageal stricture, using modified endoscopic mucosal injury grading scale. Biomed Res Int 2014;2014:919870.
[17] Tohda G, Sugawa C, Gayer C, et al. Clinical evaluation and management of caustic injury in the upper gastrointestinal tract in 95 adult patients in an urban medical center. Surg Endosc 2008;22:1119–25.
[18] Zhang C, Zhou X, Yu L, et al. Endoscopic therapy in the treatment of caustic esophageal stricture: a retrospective case series study. Dig Endosc 2013;25:490–5.
[19] Zerbib P, Voisin B, Truant S, et al. The conservative management of severe caustic gastric injuries. Ann Surg 2011;253:684–8.
[20] Ramasamy K, Gumaste VV. Corrosive ingestion in adults. J Clin Gastroenterol 2003;37:119–24.
[21] Lahoti D, Broor SL. Corrosive injury to the upper gastrointestinal tract. Indian J Gastroenterol 1993;12:135–41.
[22] 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;37:165–9.
[23] Rollin M, Jaulim A, Vaz F, et al. Caustic ingestion injury of the upper aerodigestive tract in adults. Ann R Coll Surg Engl 2015;97:304–7.
[24] Struck MF, Beilicke A, Hoffmeister A, et al. Acute emergency care and airway management of caustic ingestion in adults: single center observational study. Scand J Trauma Resusc Emerg Med 2016;24:45.
[25] Chan TY, Leung KP, Critchley JA. Poisoning due to common household products. Singapore Med J 1995;36:285–7.
[26] Gu B, Zhu W, Wang H, et al. Household hazardous waste quantification, characterization and management in China's cities: a case study of Suzhou. Waste Manag 2014;34:2414–23.
[27] Garcia-Hidalgo E, von GN, Siegrist M, et al. Use-patterns of personal care and household cleaning products in Switzerland. Food Chem Toxicol 2017;99:24–39.
[28] Nunez O, Gonzalez-Asanza C, de la CG, et al. Study of predictive factors of severe digestive lesions due to caustics ingestion. Med Clin (Barc) 2004;123:611–4.
[29] Ananthakrishnan N, Kate V, Parthasarathy G. Therapeutic options for management of pharyngoesophageal corrosive strictures. J Gastrointest Surg 2011;15:566–75.
[30] Ananthakrishnan N, Parthasarathy G, Kate V. Acute corrosive injuries of the stomach: a single unit experience of thirty years. ISRN Gastroenterol 2011;2011:914013.
[31] Subbarao KS, Kakar AK, Chandrasekhar V, et al. Cicatrical gastric stenosis caused by corrosive ingestion. Aust N Z J Surg 1988;58:143–6.
[32] Borja AR, Ransdell HTJr, Thomas TV, et al. Lye injuries of the esophagus. Analysis of ninety cases of lye ingestion. J Thorac Cardiovasc Surg 1969;57:533–8.
[33] Sugawa C, Mullins RJ, Lucas CE, et al. The value of early endoscopy following caustic ingestion. Surg Gynecol Obstet 1981;153:553–6.