Concordance between Observers for the Diagnosis and Endoscopic Classification of Esophageal Lesions Due to Caustic Ingestion in Children

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Abstract

Introduction
The accidental ingestion of caustic materials among children continues to be a public health problem, with an incidence in international reports of 15.8 / 100,000 per year. In our environment, at the Fray Antonio Alcalde Civil Hospital, this incidence has an average of 2.5 cases per month, around 30 cases per year. Objective. To evaluate the agreement between observers for the diagnosis and endoscopic classification of esophageal lesions due to the ingestion of caustics in children. Material and methods. A historical cohort study was conducted in 2,190 days with patients diagnosed with esophageal stenosis secondary to caustic ingestion during a period between 2010 and 2016. Photographic records of patients who met the inclusion criteria were recovered. Diagnostic endoscopy at the time of caustic ingestion. These reports and the fixed images of the esophagus were classified according to Zagar’s Scoring Systems for Caustic Injuries. The following variables were collected: sex, age in months, date of ingestion of caustic substance, type of ingested caustic substance, presence of complications in the acute stage, degree of initial injury according to Zagar’s classification. We reviewed the results of the esophagogram and the diagnostic endoscopy at the time of caustic ingestion and the first revision endoscopy. Later these images were evaluated by the same endoscopist and by two others, the three reports were classified according to Cohen’s Kappa coefficient, to compare the agreement between endoscopists, as well as the Kappa coefficient of Feiss to compare the general concordance entre the three endoscopists, both coefficients with a confidence interval of 95% (Kappa +/- 1.96 standard error). Statistical analysis was performed through SPSS version 19.

Results
A total of 43 patients with diagnosis of caustic ingestion at the Civil Hospital of Guadalajara “Fray Antonio Alcalde” were reviewed. The characteristics of the patients in relation to sex, 13 (30%) were female and 30 (70%) of the male sex. The average age was 34.5 months, with a range of 12 to 96 months. 42 patients for caustic soda (98%) and one patient with burn by muriatic acid (2%). First-time endoscopy was performed within the first 18-24 hrs after the injury, they did not present any complications in the acute stage, and they had the diagnosis of caustic burn according to the Scoring Systems for Caustic Lesions of Zagar. Identifying 2 patients with grade I burns (4.6%), 8 patients with grade IIa burn (18.6%), 14 patients with grade IIb burn (32.5%), 17 patients with burn IIIa (39.5%) and 2 patients with burn IIIb (4.6%). A total of 63 images were obtained, which were identified according to the predominant pattern of lesion due to caustic ingestion based on Zargar’s classification. Each image was displayed in a time of 20-30 seconds, with the total evaluation ending in an average of 30 minutes. The variability of concordance between pairs of endoscopists was compared when integrating the 3 endoscopists, a Kappa Feiss Coefficient of 0.3948 was obtained, with a standard error of 0.0402 and a confidence interval of 95% from 0.3160 to 0.4736. With this tool the kappa coefficient observed for the degree of esophageal burn injuries according to the Zargar Classification was 0.6583 (good concordance strength) for grade I, 0.4393 (moderate concordance force) for grade II a, 0.3000 (force low concordance) for grade II b, 0.4674 (moderate agreement strength)
for grade III a, and 0.0950 (agreement strength without agreement) for grade III b.

**Discussion and conclusion**
The overall agreement (Kappa Feiss) regarding the decision of the presence / absence of mild / severe esophageal lesions (grade I, II a vs. grade II b, III a, III b) had a moderate reliability, but poor for leveling fine of each of the grades, with the strength of negligible agreement (kappa 30 0.0950) for grade IIIb, low (kappa 0.3000) for grade IIb, moderate for grade Ila (kappa 0.4393) and IIIa (kappa 0.4674) and good for grade I (kappa 0.6385). We believe that endoscopy is a mandatory and effective technique that should be performed to prevent unnecessary hospitalization and medication, as well as to plan initial treatment and to predict patients who are at risk of developing esophageal stenosis and / or obstruction of the exit gastric and can be performed without complications in expert hands.

**Keywords:** Agreement for Diagnosis and Classification, Caustic, Esophagus, Children

**Introduction**
The accidental ingestion of caustic materials among children continues to be a public health problem, with an incidence in international reports of 15.8 / 100,000 per year. The incidence of these accidents was estimated in international reports to be as high as 15.8 / 100,000 per year. In the USA, an annual incidence of between 5,000 and 15,000 cases is estimated; of which 50-80% occur in childhood [1].

In our environment, at the Fray Antonio Alcalde Civil Hospital, this incidence has an average of 2.5 cases per month, around 30 cases per year. Giving rise to short and long-term associated complications, including bleeding, perforation, systemic complications, esophageal stenosis, fistula, obstruction of the gastric outlet and cancer. The rapid assessment of the severity of the injury is very important, since the prognosis depends on the early application of an adequate treatment. In this regard, esophagogastroduodenoscopy (EGD) is the most effective method to establish the severity of the injury. However, this endoscopic evaluation is often subjective, with the use of scoring systems that have been developed for adult patients, such as the Zargar Classification for the degree of esophageal injury by caustics, yielding contradictory results regarding the validity in pediatric patients. Therefore, the objective of this study was to evaluate the agreement between observers for the diagnosis and endoscopic classification of esophageal lesions by ingestion of caustics in children.

There are pH values that we consider critical. The pH above which alkaline substances have a greater capacity to produce caustic injuries is equal to or greater than 12, while acidic substances can produce esophageal damage with a pH lower than 4 [2-5]. The acids produce a necrosis by protein coagulation, with loss of water, forming a firm and protective eschar that makes penetration difficult, except in high concentrations. The alkalis provoke a necrosis by liquefaction, with denaturation of proteins, saponification of fats and capillary thrombosis. The retention of water that causes increases liquefaction, with denaturation of proteins, saponification of fats and capillary thrombosis. These reactions are what favor the deepening of the lesions [2, 3, 6, 7]. It is more frequent that acids are related to gastric lesions than alkalis, but in reality alkalis also cause severe gastric lesions, because due to the associated pyloric spasm the caustic substance is retained in the gastric cavity which increases the lesion [8]. The severity of the lesions is variable since the overall mortality is between 3% and 12% and in cases with suicide purposes the mortality can be as high as 66%. With regard to the morbidity of these patients, 40% result in sequelae in the esophagus, which are characterized by fibrosis and stenosis [7, 9, 10]. when they are significant, they involve many years of functional disability, treatments that in many cases are prolonged, costly and debilitating of the physical and emotional integrity of both the patient and their family members because the rehabilitation of these patients is based on esophageal dilatations involving intravenous sedation and inhaled or general anesthesia every 2 to 3 weeks for months or years and finally between 5 to 10% will require esophageal replacement. In addition to the above, it has been described that after the ingestion of caustics; there is the possibility of malignant transformation to esophageal cancer, on average 30 years after the ingestion of caustics [2-6].

**Material and method**
A historical cohort study was carried out, based on the endoscopy unit of the Pediatric Surgery Service 6 in the population constituted by all patients admitted with a diagnosis of esophageal stenosis secondary to caustic ingestion from 2010 to December 2016, in the Hospital Civil de Guadalajara “Fray Antonio Alcalde” (HCGFAA) which provides health services to urban population, open, with limited economic resources, low educational level and no social security. The size of the sample was determined by the frequency of the main variable, a study that took the patients of 7 years (partial retrospective), with an estimated patients per year and therefore around 180 patients, which is estimated that around 40% will progress to esophageal stenosis and 5 to 10% will end up in surgery (average 7.5%), accepting an error of 5% and a confidence level of 95%, 49 patients are required. The sample was constituted by the photographic archives of 43 patients who fulfilled the inclusion criteria, of having diagnostic endoscopy within the first 24 hrs of caustic ingestion. These reports and the fixed images of the esophagus were classified according to the Scoring Systems for Caustic Lesions of Zagar (Table 1). The following variables were collected: sex, age in months, date of ingestion of caustic substance, type of ingested caustic substance, presence of complications in the acute stage, degree of initial injury according to Zagar’s classification. We reviewed the results of the esophagogram and the diagnostic endoscopy at the time of caustic ingestion and the first revision endoscopy. Afterwards, these images were evaluated by the same endoscopist and by two others; the three reports were classified according to Cohen’s Kappa coefficient, to compare the agreement between endoscopists, as well as the Feiss Kappa Coefficient to compare the general concordance between the three endoscopists, both coefficients with a confidence interval of 95% (Kappa +/- 1.96 standard error) (Tabla 2). Measures of central tendency (mean and median), and dispersion (standard deviation, maximum - minimum) for the quantitative variables were calculated. The Kappa index of Cohen and Kappa de Feiss was used to measure the agreement between observers. Statistical analysis was performed through SPSS version 19.
Tabla 1: Sistema de puntuación endoscópica Zargar para diagnóstico de lesión esofágica

<table>
<thead>
<tr>
<th>Grado</th>
<th>Descripción Endoscópica</th>
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<tr>
<td>Grado I</td>
<td>Edema, eritema, hiperemia de la mucosa.</td>
</tr>
<tr>
<td>Grado IIa</td>
<td>Ulceras superficiales, lineales, erosiones, friabilidad, ampollas, exudado, membrana y hemorragia.</td>
</tr>
<tr>
<td>Grado IIb</td>
<td>Grado 2ª + Ulceras circunferenciales o profundas.</td>
</tr>
<tr>
<td>Grado IIIa</td>
<td>Áreas pequeñas y focales de múltiples ulceraciones y necrosis de coloración marrón-negruzca o grisácea.</td>
</tr>
<tr>
<td>Grado IIIb</td>
<td>Áreas extensas de necrosis.</td>
</tr>
<tr>
<td>Grado IV</td>
<td>Perforación.</td>
</tr>
</tbody>
</table>

Tabla 2: Interpretación Kappa

<table>
<thead>
<tr>
<th>kappa</th>
<th>grado de acuerdo</th>
</tr>
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<tbody>
<tr>
<td>&lt; 0</td>
<td>sin acuerdo</td>
</tr>
<tr>
<td>0 - 0.2</td>
<td>insignificante</td>
</tr>
<tr>
<td>0.2 - 0.4</td>
<td>bajo</td>
</tr>
<tr>
<td>0.4 - 0.6</td>
<td>moderado</td>
</tr>
<tr>
<td>0.6 - 0.8</td>
<td>bueno</td>
</tr>
<tr>
<td>0.8 - 1</td>
<td>muy bueno</td>
</tr>
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</table>

**Results**

During the study period, sufficient information was collected for the research in 43 cases with recovery of 63 images. The characteristics of the patients in relation to sex, 13 (30%) were female and 30 (70%) male. The average age was 34.5 months, with a range of 12 to 96 months. (Graph 1) The causative agents of esophageal caustic lesions with subsequent esophageal stenosis were: 42 patients for caustic soda (98%) and one patient with muriatic acid burn (2%) (Graph 2). Of the patients who underwent first-time endoscopy within the first 18-24 hours after the injury in our service, they did not present any complication in the acute stage, and they had the diagnosis of caustic burn according to the score for Zagar caustic injuries, identifying 2 patients with grade I burns (4.6%), 8 patients with grade IIa burn (18.6%), 14 patients with grade IIb burn (32.5%), 17 patients with IIIa burn (39.5%)) and 2 patients with burn IIIb (4.6%) (Graph 3). In figure 1 you can see some images of these injuries. Of these patients after diagnostic endoscopy, 20 patients required gastrostomy, corresponding to lesion grades II b, III a, III b Zagar. A total of 63 images were obtained, which were identified according to the predominant pattern of lesion due to caustic ingestion based on Zargar’s classification. Each image was shown in a time of 20-30 seconds, with the total evaluation ending in an average of 30 minutes (Figure 1).

**Gráfica 1**: Género

**Gráfica 2**: Agente Caústico

**Gráfica 3**: Clasificación Zargar en Endoscopia Inicial

**Figura 1**: Lesiones Observadas

The variability of concordance between pairs of endoscopists was compared, in group 1 (endoscopist 1 / endoscopist 2) the Coefficient Kappa Cohen (Kappa unweighted) was 0.2764, with a standard error
(ES) of 0.0788 and a Confidence Interval (CI) of 95% from 0.1219 to 0.4310 resulting in a low match strength; a heavy Kappa Cohen coefficient (kappa Weighted) of 0.4851 with a standard error (ES) of 0.0627 and a Confidence Interval (CI) of 95% with ranges from 0.3623 to 0.6079 resulting in a moderate concordance force (Table 3). In group 2 (endoscopist 1 / endoscopist 3) the unweighted Kappa coefficient (Kappa unweighted) was 0.4384, with a standard error of 0.0812 and a 95% Confidence Interval of 0.2793-0.5976, resulting in a matching force poor; a heavy Kappa coefficient (kappa Weighted) of 0.5771, with a standard error of 0.0715 and a Confidence interval of 95% of 0.4369-0.7173, resulting in a moderate concordance force (Table 4).

And in group 3 (endoscopist 2 / endoscopist 3) the unweighted Kappa coefficient (Kappa unweighted) was 0.4869, with a standard error of 0.0820 and a Confidence Interval of 95% of 0.3262-0.6476, resulting in a strength of moderate agreement; a heavy Kappa coefficient (kappa Weighted) of 0.5896, with a standard error of 0.0717 and a Confidence interval of 95% from 0.4490 to 0.7302, resulting in a moderate concordance force (Table 5). Finally, when integrating the 3 endoscopists, a Kappa Feiss Coefficient of 0.3948 was obtained, with a standard error of 0.0402 and a confidence interval of 95% from 0.3160 to 0.4736. With this tool the kappa coefficient observed for the degree of esophageal burn injuries according to the Zargar Classification was 0.6585 (good concordance strength) for grade I, 0.4393 (moderate concordance force) for grade II a, 0.3000 (force low agreement) for grade II b, 0.4674 (moderate agreement strength) for grade III a, and 0.0950 (agreement strength without agreement) for grade III b (Table 6).
Discussion and Conclusions
Accidental ingestion of caustic agents can cause devastating damage to children. Unlike adults, most children ingest caustic materials by accident, and usually stop as soon as they feel uncomfortable. However, it is almost always too late to avoid resulting esophageal injuries. Strong alkalis are present in a wide range of household cleaning products and industrial beauty products, often attractively packaged and easily accessible to children, both at home and on low store shelves. In our environment, the main caustic agent involved in esophageal lesions is caustic soda, as presented in our study; this is due to the poor legislation that exists in our country regarding the sale and commercialization of it; There is no regularization regarding the concentration and packaging that caustic products should have, which leads to a greater frequency and severity of the type of injuries compared to that reported to developed countries [9]. The largest risk group for accidental caustic ingestion is children under 5 years of age, and most study groups agree that the incidence peaks are around 2 years of age, when children develop self-help skills. Location, but they are poor discriminators between harmless and harmful substances. In our study, it was predominant in men with an average age of 31.4 months, similar to previous reports from national and international literature [10].

Late complications of caustic ingestion are closely related to the depth and extent of esophageal and / or gastric lesions. Several approaches and treatment modalities are recommended in affected children. However, to estimate the risk of stenosis formation, the presence of esophageal and gastric damage must be documented. At this point, endoscopic classification is important for prognosis and management. In general, grade 0 and 1 lesions do not develop late sequelae, such as esophageal stenosis or obstruction of the gastric outlet, whose incidence increases with the severity of the lesion. In addition, the degree of esophageal injury at endoscopy is an accurate indicator of systemic complications and death, with each increase in the degree of lesions correlated with a 9-fold increase in the morbidity and mortality [8, 11, 12]. Studies conducted in adults regarding the role of endoscopic classification to predict complications after esophageal / gastric lesions due to caustics, such as that of Cheng et al. confirm the Zargar Classification as a useful tool. However, in the pediatric studies there was no consistency in the use of the same classification system, in the study by Riffat and Cheng, they used the Estreta System; in that of Temiz et al [10, 12]. The Di Costanza System; and Rodríguez Guerineau et al [13]. The Zargar system; as well as the coefficient of agreement between observers of the same ones is not mentioned, which makes it difficult to establish a consensus in the pediatric age so that we speak of the same degrees of esophageal lesion and allow performing meta-analysis between the study groups [14]. In the present study, patients evaluated from the beginning in our institution, 4.6% had burns grade I, 18.6% grade IIa, 32.5% grade IIb, 39.5% grade III to (39.5%) and 4.6% with burn III b. Of these patients, 46% underwent gastrostomy for feeding and rehabilitation purposes; these figures show a trend similar to that reported in the international literature [15-17]. In this regard, emergency surgery should be planned according to the
endoscopic degree of burn, although isolated black eschar does not always indicate full thickness lesions and the need for immediate surgery, these patients may deserve further evaluation and close observation. Recently, some publications have raised the correlation between endoscopic findings and the extent of necrosis, where the decision to perform emergency surgery was based exclusively on these, which led to unnecessary surgery in 15% of cases. This suggests the need to improve the criteria for early surgery [11].

Regarding the variability of agreement between observers for the diagnosis and endoscopic classification of esophageal lesions by caustic ingestion in children, using the Zargar System, which was the purpose of the present work, despite the fact that the sample size was not reached, it is important to highlight that the images required for the application of the kappa coefficient could be recovered, since a single patient could present more than 2 types of injuries. The overall agreement (Kappa Feiss) regarding the decision of the presence / absence of mild / severe esophageal lesions (grade I, II a vs. grade II b, III a, III b) had a moderate reliability, but poor for leveling fine of each of the grades, with the strength of insignificant agreement (kappa 0.0950) for grade IIIb, low (kappa 0.3000) for grade IIb, moderate for grade IIa (kappa 0.4393) and IIIa (kappa 0.4674) and good for grade I (kappa 0.6585). The agreement between observers (kappa Cohen) comparing the endoscopists in pairs was moderate (kappa 0.4869) for endoscopist 2 / endoscopist 3 and endoscopist 1 / endoscopist 3 (kappa 0.4384) and poor for endoscopy 1 / endoscopy 2 (kappa 0.2764). However, in the group evaluation of the characteristics of the lesions there is no dispersion in the classification grades of the lesions, showing minimal variability (one degree above vs one degree below), which means that among the 3 endoscopists there may be a consensus axis for the final diagnosis of the lesion. In this regard we can comment that the method to carry out qualitative measures in clinical practice is far from perfect. The characteristics of an ideal diagnostic method include reproducibility and a significant absence of interobserver variability [18]. The concordance studies allow identifying the degree of agreement among several observers and the consistency of the observer, whose measurements can be analyzed to conclude whether a diagnostic procedure may or may not be reproducible in a population. The above is particularly useful in the field of endoscopy, since there is a number of classifications whose interpretation varies from observer to observer (19) Pandolfini and colleagues reported the degree of interobserver and intraobserver agreement in the identification of degrees of esophagitis in two types of classifications between experienced endoscopists and in training [20].

The interobserver concordance obtained was 0.43 and 0.54 in the group of endoscopists in training and experienced respectively. The intraobserver concordance was similar, so the author concludes that the experience of the endoscopist intervenes in the results. In a study like ours there are many factors that influence the results as artifacts that alter the interpretation even though an attempt is always made to obtain high quality images. We recognize the fact that we use only photographs for the agreement between observers, as well as that an arbitrary period of time was assigned to perform the examination of each image, 30 seconds on average, but the time has not yet been established. For it. In previous studies there have been periods of time ranging from an interval of 20 seconds to all the time they needed to give their diagnosis. Another limitation that may be present is the fact that the interpretation is very subjective and depends on the observer, which could lead to an overestimation or underestimation of the lesions [21-25]. In conclusion, we believe that endoscopy is an obligatory and effective technique should be performed to prevent unnecessary hospitalization and medication, as well as to plan initial treatment and to predict patients who are at risk of developing esophageal stenosis and / or obstruction of the gastric outlet and can be performed without complications in expert hands.

Regarding the results of this study, we can conclude that Zagar’s classification in the pediatric case in our setting showed a low concordance force in the group analysis (kappa Feiss), and moderate-low in the paired analysis (Kappa Cohen). Therefore, in the present study, referring to our hospital environment, the assessment of two or more observers of endoscopic studies in the case of caustic esophageal lesions in children does not increase the diagnostic reliability. However, the group evaluation of the characteristics of the lesions showed minimal variability (one degree above vs one degree below), which means that among the 3 endoscopists there may be a consensus axis for the final diagnosis of the lesion. We suggest that in addition to making this axis of consensus among endoscopists in our environment, other diagnostic resources should be implemented that allow a better concordance coefficient in the initial evaluation, such as conventional and / or electronic chromoendoscopy or assessment with Esophageal Ultrasound [26, 27]. Which will allow a better decision making regarding medical management, emergency surgery and the use of other modulators of healing such as mitomycin from the initial endoscopy? We believe that we should continue to deepen the study of this pathology; In order to identify other variables that influence the rate of complications and the final prognosis of the patient.

Declaration of conflicts of interest
The authors declare that for this investigation no material or financial support was received that generates conflicts of interest.

References

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