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Caustic ingestion in children—A review

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ABSTRACT

Various domestic or industrial chemicals may cause significant upper aerodigestive tract burns. Preventive measures should be up-scaled, especially in the developing world, to reduce the epidemic of accidental victims, largely unsupervised preschool children. External signs do not predict degree of injury. Non-invasive diagnostic screening includes radio-nuclear imaging, but early oesophago-gastroduodenoscopy remains the standard to predict stricture formation from circumferential submucosal scarring. Serial dilation is the mainstay of oesophageal stricture therapy, with oesophageal replacement reserved for severe refractory strictures. Intra-lesional steroid or mitomycin C may decrease the dilatations required for severe strictures, although long-term effects are unknown. Risk of secondary oesophageal carcinoma mandates long-term surveillance.

Introduction

Preventive measures have made significant impact on reducing caustic injuries in many countries. It is, however, still a goal that needs to be realised by many developing countries. Most caustic injuries are seen in countries where prevention is still lacking due to social, economic and educational variables. Half to 80% of the injuries are seen in children.[1,2] These are typically accidental in nature. This is in contrast to ingestion by adults which is often suicidal and frequently life-threatening. True prevalence of caustic injuries in children is not known but limited data available supports the large scale of the problem, which is a major public health issue.

The aim of this article is to discuss impact of caustic injuries and its sequelae, particularly in low and middle income countries (LMIC), to describe well-established treatment modalities and to look into the controversial management options.

Epidemiology

Ingestion of highly alkali or acidic substances is a major cause of morbidity and mortality worldwide, especially in developing regions. Victims are largely unsupervised preschool children.[1,2] Most taste or drink household cleaning agents due to curiosity or while searching for food or drink. Toddlers are most at risk, averaging 3 years of age at ingestion.[3] Risk factors for caustic ingestion in children include male gender,[4–6] attention-deficit/hyperactivity disorder symptoms,[4] lower parental education status,[4,7] young maternal age,[8] lack of parental supervision[8] and rural abode.[9] Incidence is reported at 5–518 paediatric caustic ingestion events per 100,000 populations per year, although noting a steady decline in higher income countries.[10–12] The majority of ingestions occur in children younger than 5 years old, and are totally preventable. Toxic ingestion in cases older than 5 years old is suspect and ingestion in adolescents is usually intentional. Mortality is rare but morbidity is devastating and in some cases, life-long.

A total of 20–40% of patients ingesting caustic substances may incur oesophageal injury.[13,14] Accidental ingestion of substances with an alkali (pH $>$ 11.5) or acid (pH $<$ 2) may cause significant burns to the cheeks, mouth, oropharynx, oesophagus and stomach and rarely duodenum, as well as airway.[15] Oxidising agents and phenols are not strong acids or alkalis but can burn exposed skin and gastro-intestinal mucosa, and also potentially cause other toxic effects. Tables 1 and 2 list common caustic agents and their attributes.[5,16–21]

Causative substances vary from region to region. Novel domestic cleaning product packaging (e.g., spray bottles and capsules) can introduce new sources of risk.[12,22] Industrial agents rival domestic agents in frequency of ingestion outside Europe and North America.[3] Oxidising substances such as peroxides or chlorine bleaches are the most commonly ingested substances,[5,23] although they rarely cause long-term gastro-intestinal sequelae. Overall, 7–25% of ingested substances lead to serious long-term gastro-intestinal morbidity with stricture formation.[5,13] Deep

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Table 1
Strong alkalis and acids commonly implicated in paediatric caustic ingestion injury. Grey highlights substances with high risk for trans-mucosal injury.

Type	Caustic agent	Chemical formula	pH (at 25°C at maximum molar concentration of H^+/ OH^-(N), unless otherwise stated)	Common names	Household use	Incidence of associated strictures (concentration dependent)
Strong alkalis	Sodium hydroxide	NaOH	12.9 (100 mM) up to 14 (N)	Lye, caustic soda	Industrial detergents; drainpipe and oven cleaners ("degreasers"); hair relaxers; alkaline disk cell ("button battery")	Caustic soda crystals (46% concentration): 75%; oven cleaners 5–15% concentration: ~10–30%
	Potassium hydroxide	KOH	12.9 (100 mM) up to 14 (N)	Potash; also called lye	As above, including "non-lye" hair relaxers	~11%
	Lithium hydroxide	LiOH	14		Non-lye hair relaxers	None reported
	Calcium hydroxide	$Ca(OH)_2$	12.46	Lime; whitewash	Industrial, food preparation, paint, depilators etc.	
	Trisodium phosphate	Na_3PO_4	11.9 (1% aqueous solution) to 12.12 (at 100 mM)	Sodium phosphate	Cleaning agents and detergents including automatic clothes washing machines and dishwasher detergents	
		NH_4OH(aq)	Domestic cleaning agents; pH 6.5–10; hair relaxants: pH > 10; burns ≥ 5% concentration; 10% (industrial) concentration: pH13	Ammonium water	Industrial; Household cleaning agents, thioglycolate/sulphite hair relaxers	Up to 50% with ammonium chloride solution
	Disodium carbonate	Na_2CO_3	11.4 (1% aqueous solution) to 11.7 (10% aqueous solutions)	Sodium carbonate, soda ash, and washing soda	Soaps and detergents	
Strong acids:	Acetic acid	$C_2H_4O_2$	2.88 (100 mM)	Vinegar	Culinary and household cleaning agent	None
	Citric acid	$C_6H_8O_7$	2.2 (0.1 N); 3.2 at 1 mM		Automatic dishwasher and household cleaning agent; culinary	None
	Phosphoric acid(5)	H_3PO_4	Domestic preparations >2 Industrial solutions >85% corrosive; pH at 100% is 1.08		Household and industrial cleaning agents; derusting agent and dental use	
	Hydrochloric acid	HCl	1.08 (100 mM)		Limescale dissolver, swimming pool acid	~2%

Table 2
Oxidising agents and phenols commonly implicated in paediatric caustic ingestion injury.

Type	Caustic agent	Chemical formula	pH	Common names	Household use	Comment
Oxidising agents	Hydrogen peroxide	H_2O_2	5.3 (10% solution)	Peroxide	Fabric stain removers, hair dyes, domestic disinfectants and deodorisers	Domestic preparations (≤ 10%): mild gastro-intestinal irritant only Industrial preparations: haemorrhagic gastritis, gas embolism, hollow viscera perforation from gas accumulation
	Sodium hypochlorite	NaClO	Domestic preparations (~ 3.5% concentration): 7–11 Industrial concentrations (~ 40%): up to 13.5	Bleach	Household and industrial bleaching agents, disinfectants and deodorants	Majority only mucosal hyperaemia; reports of strictures (industrial strength) extremely rare
	Calcium hypochlorite	$Ca(ClO)_2$	As above	HTH (high test hypochlorite)	As above	
	Potassium permanganate	$KMnO_4$	6.5–9.5	Condy's crystals	Antiseptic, disinfectant and hair dyes	Oropharyngeal burns main sequelae
Phenols	Phenol	C_6H_5OH (hydroxyl-benzene ring)	6.0	Carbolic acid	Disinfectant, insecticide, oral antiseptic/analgesic preparations and cosmetics	Neurotoxic; causes methaemoglobinaemia, hypovolaemic shock
	Salicyclic acid	$C_6H_6O_3$	2.4	Hydroxybenzoic acid, Aspirin®, and Disprin®	Anti-inflammatory, exfoliator and bacteriostatic	Respiratory depression, renal and nervous toxicity

burns resulting in strictures are due to alkali agents in a third to three quarters of caustic ingestion,[3,5,6] followed by acids.

Caustic exposure became a significant problem with the use of lye (sodium hydroxide) in household cleaners after the turn of the 19th century. Caustic soda (consisting of sodium hydroxide crystals) is predominantly used in manufacturing soap in the home; stronger concentrations are used in drain and oven cleaners. Sodium hydroxide causes about a third of oesophageal strictures.[24] A total of 10–75% of children ingesting it developed strictures, depending on the concentration involved.[5] This led to strict legislation in some countries, restricting domestic availability and concentrations and halting lye injuries.[9,25] Concomitantly, developed countries have seen a rise in automatic dishwasher detergent ingestion (over half of caustic ingestion cases in one series),[25] although significant resultant burns are less common at 2.7%.[10] Concentrated preparations in agricultural use put children in rural communities at more risk of severe caustic injuries.[9]

Acid ingestion is much more prevalent in Europe and Asia than in Africa, the Americas and Oceania.[3] Stricture formation after acid ingestion is reported at 2.9–15.3% in children,[5,26] with most series reporting lower stricture rates compared to alkali ingestion. Common household vinegar was responsible for about half of acid ingestion in Finland,[25] but strictures are not reported from this relatively weak acid. Other commonly ingested acids include hydrochloric and salicylic acid, with oesophageal strictures reported in 2% and a few case reports respectively.[5,27]

Pathophysiology

The depth of injury depends on the tissue concentration of the caustic substance, which is difficult to assess from the history, even if the causative agent and its concentration is known.[28] An acid usually forms an eschar of burnt tissue from protein coagulation (coagulation necrosis) which may protect against deeper tissue penetration. Their sour taste may also limit accidental intake. Alkaline agents disrupt both proteins and fats, combining with them and destroying cell architecture, a process known as liquefactive necrosis. Higher surface tension of alkalis can increase focal tissue concentration.[29] Tissue destruction can continue from the mucosa through muscle wall layers until the alkali is neutralised. In addition, thrombosis in blood vessels reduces perfusion to burnt tissue.[28] Inflammation and necrosis may progress due to expansion of the ischaemic zone around the burnt tissue. Injury from liquids may be more anatomically extensive, whereas solid or particulate agents cause more focal injures that may penetrate much more deeply into tissue due to prolonged contact time. Acid in the stomach neutralises alkalis.[29] However, although it is generally accepted that alkali substances usually injure the oesophagus and acid often damages the stomach, it is not infrequent to see oesophageal injuries with acid ingestion and vice versa.[30] Severe gastric injuries are reported in 14% of acid and 2.9% of alkali injuries in one study.[31]

Four to seven days after ingestion, mucosal sloughing and bacterial invasion become evident.[32] During this period, perforation can develop in full-thickness injuries. Oesophageal repair usually starts at day 10 after the injury.[28] It is recommended to avoid endoscopy between 5 and 15 days after injury due to reduced tensile strength. Scar retraction begins by the third week by fibroblast proliferation. Associated gastro-oesophageal reflux contributes to ongoing scar formation and stenosis. Mucosal re-epithelialization begins during this period and is usually completed by the sixth week after injury. This process of scar formation may lead to strictures and shortening of the oesophagus if a large proportion of the diameter is involved to the depth of the muscularis propria or deeper.

Although infrequently seen, full-thickness hollow viscera perforation can lead to death if early surgical intervention does not successfully limit sepsis and ensuing multi-organ failure. Caustic erosion into adjacent viscera can present, sometimes after a delay of days up to 3 weeks, with perforation or fistulisation into the tracheobronchial tree, aorta or other vessels, colon, small bowel, pancreas and gallbladder.[1]

Reduction and oxidation agents as well as phenols can also burn tissue, but fortunately deep tissue injury is rare. There are extremely few reports of oesophageal strictures from chlorine bleach ingestion in adults,[33,34] and none in children.[5]

Significant focal burns from an ingested disk cell ("button battery") impacted within the oesophagus can develop within a couple of hours, necessitating urgent endoscopic removal. While alkaline cells contain small amounts of highly caustic agents, their hydroxide concentration is lower than what is produced by the intense hydrolytic process at the narrow negative pole of a cell in contact with tissue.[35] Leakage of the caustic contents of an accidentally ingested battery is rare under 48 h of ingestion, despite the corrosive effect of stomach acid on the casing. These are thus largely electrical burns (especially in the case of high voltage lithium-ion cells)[36] and will not be discussed further here.

Primary prevention

Nearly all paediatric injuries are due to accidental ingestion[6] with 86–90% occurring within the home environment or in directly adjacent surroundings.[8] Containers are frequently found unmarked and within reach of children, without child-proof seals.[6,8] Legislation banning domestic retail of sodium hydroxide-based cleaning agents[25] or limiting concentration of strong bases in domestic preparations,[1] has significantly reduced incidence and severity of injuries in some countries. Legislated safety requirements may include clear package labelling, listing dangerous ingredients and information on first aid in case of ingestion or skin contact, as well as poison help-line telephone numbers. Child-proof bottle tops and spray-bottle safety catches should be manufacturing norms for the domestic market, and preferably in agricultural and industrial applications too.[9] Decanting poisonous agents into cool drink containers is a frequent cause of subsequent paediatric caustic ingestion, as solutions are often odourless and colourless, resembling water. Public Health education programmes can further decrease the epidemic of caustic-related injuries, which occur mostly in the developing world. For example, novel influx of laundry detergent capsules has led to a significant number of severe associated caustic ingestion injuries, due to their bright attractive colours and lack of parental awareness.[22,37] Non-governmental organisations such as Child Safe South Africa have been actively promoting preventive measures during the past 30 years with promising results. We have noted a change in our oesophageal replacement indications over the years. While the majority of our colonic interpositions were done for caustic oesophageal injury initially,[38] during the past 10 years patients undergoing colonic interposition for caustic injury have declined to 8/22 (36%).

Presentation

A history of substance ingestion is the most common presentation. Symptoms depend on the form, amount and strength of the caustic substance. Crystal and solid forms tend to cause oropharyngeal burns. Conversely liquids tend to be swallowed and create oesophageal injury.

Half to two-thirds of children are asymptomatic after reported caustic ingestion.[39] Absence of signs is regarded by some as indicative of no or minimal injury, with no need for diagnostic endoscopy,[5,13,39–41] although oesophageal lesions were reported in 35% of asymptomatic patients in one series.[31] Inflammation and associated obstructive symptoms may take 24–48 h to develop, and these patients should still be observed over this period.

Airway injury is reported in 6–18%[6,42] of children with caustic ingestion. Oropharyngeal burns and oedema may be present, and hoarseness, stridor, dyspnoea, tachypnoea and wheezing or crepitations on auscultation may develop. Airway involvement may be due to aspiration at the time of ingestion or with subsequent emesis, due to oedema and caustic burns in the pharynx, and also due to volatile agents ingested with the caustic substance. If airway injury is severe, it may require emergency tracheostomy.

Although rare (reported at 0.2%)[43], transmural oesophageal or gastric necrosis and ensuing mediastinitis or peritonitis may present with fever, tachycardia, severe retrosternal or abdominal pain, haemorrhage as well as sepsis and organ dysfunction. Urgent surgical exploration is required. It must be kept in mind that oesophageal perforation can happen any time during the first 2 weeks after ingestion.

Drooling, dysphagia and epigastric pain indicate potential gastro-intestinal involvement. Drooling (63%)[42] and inability to swallow are the most common symptoms and children with these symptoms warrant further investigation to confirm injury severity. Vomiting is also found in about half of cases[5,42] However, absence of vomiting, drooling and oral burns do not exclude oesophageal involvement. Oral mucosal injury is absent in 12% of patients with oesophageal injury,[6] and stricture development has been reported in 1% of children with no oral signs of injury.[5] Haematemesis and multiple symptoms have been suggested to be indicative of high-grade injury.[39] Prolonged symptoms of drooling and dysphagia may also predict oesophageal scarring.[25] However, external signs and symptoms also cannot reliably predict degree of injury. Although there are studies showing increased likelihood of oesophageal injury with three or more symptoms,[40,44] some studies failed to show this correlation. This is explained by decreased motility and increased transit time during the first few days to weeks after ingestion with no severe injury. However, once the oesophagus is injured, resulting fibrosis and abnormal oesophageal peristalsis may result in dysphagia. This can be seen with or without stricture development.

Systemic effects

Ingested agents with pH between 2 and 11.5 may cause mild to moderate gastro-intestinal irritation, with superficial (mucosal) injury. Deep to full-thickness injury is rare. Vomiting and diarrhoea, as well as haemorrhagic gastritis with epigastric pain, may develop. Significant gastro-intestinal burns leading to long-term sequelae are rarely reported. Intensive systemic support may, however, be required due to effects of systemic absorption (e.g., methaemoglobinaemia and neurotoxicity from phenols, for example, salicyclic acid)[19,20,45] or pulmonary symptoms (e.g., pneumonitis associated with volatile hydrocarbons such as found in paint thinners), etc. Activated charcoal via nasogastric tube may be indicated in some agents (e.g., phenols) to limit further systemic absorption,[46] but will compromise the accuracy of endoscopic evaluation of the injury. An ingested substance may contain multiple potentially caustic agents, and consulting a poison centre database is useful to clarify the exact contents if unclear from the history and package labelling, and prioritise treatment.

Home first aid measures

The causative agent should immediately be removed and identified if possible. A poison telephone help-line may aid

identification of caustic contents. Vomiting should never be induced, as it can increase caustic exposure,[5] but can occur spontaneously due to gastric irritation. A neutral liquid (preferably water, but milk may be considered) should be given to drink if possible to help neutralise the agent,[47] taking care not to stimulate vomiting. Urgent medical attention should be sought, particularly if items in Table 1 are ingested.

Acute phase treatment

The majority of children with a history of caustic ingestion (up to 70%[48]) are asymptomatic and can be observed for 12–48 h, depending on the nature of the substance ingested.

Those with airway symptoms may require supplementary oxygen. Temporary endotracheal intubation was reported necessary in up to 18%.[6] Long-term tracheostomy may be required in about 1%.[49]

Symptomatic patients are kept nil per mouth until further investigations have been performed, on intravenous maintenance fluid.

Broad spectrum antibiotics are frequently prescribed routinely in the acute phase,[6,50] but not universally,[5,51] based on previous animal studies showing increased granulation with bacterial invasion of disrupted mucosa.[52] Clinical evidence does not support its routine use.[53] Antibiotic therapy is mandated if there are signs of hollow viscous perforation, and may be given empirically for patients with high-grade pyrexia with suspected bacteraemia from bacterial translocation or aspiration pneumonia or pneumonitis. Antibiotic prophylaxis may be considered at initial endoscopy due to the small risk of perforation and secondary bacteraemia.[31] Antibiotics given in conjunction with steroids do not mitigate the immunosuppressive effect of steroids.[54]

Special investigations:

- *Erect chest X-ray* is used to screen for free mediastinal or subdiaphragmatic air from oesophageal or gastric perforation, and also to assess lung fields for evidence of associated pneumonitis/aspiration pneumonia.
- *A technetium-labelled sucralfate scan*, described by our institution in 2001,[55] is currently the only non-invasive screening investigation to determine potential oesophageal injury. ^{99m}Tc-labelled sucralfate adheres to the injured and inflamed mucosa, which can be detected as residual activity on nuclear scintigraphy. Results have indicated that upper gastro-intestinal endoscopy, which currently is the gold standard in establishing injury, can be avoided in almost half of the cases with a history of caustic ingestion. It is recommended that all patients found to have positive sucralfate scans indicating retained activity in the oesophagus should undergo endoscopic assessment under general anaesthesia to identify the degree of injury. This screening is safe and cost-effective, with a positive predictive value of oesophageal mucosal injury of 47%.[56]
- Early *oesophago-gastroduodenoscopy* remains the gold standard in establishing absence or presence of oesophageal injury as well as estimation of the grade of injury. We recommend endoscopy in children who swallowed potent caustic substances such as drain cleaners, oven cleaners and hair straighteners. It is our practice to perform endoscopy under general anaesthesia for all children with positive sucralfate scans during the first 24–48 h of admission. Other indications for endoscopic evaluation include acute respiratory complications,[24] with symptoms such as stridor. Endoscopic grading of injury is shown in Table 3.[26,40,41,57,58] This allows prediction of risk of long-term stricture formation from partial or circumferential scarring.

There are no studies confirming the accuracy and documenting potential complications of early compared to late endoscopy. Endoscopy under 12 h after injury may underestimate the injury.[53] We recommend not delaying the endoscopy beyond 48 h from the time of injury to minimise the potential risk of perforating the oesophagus, which might be entering its weakest stage during the tissue healing phase. Reports of safe endoscopy after 48 h from injury[6] underline the lack of clinical evidence regarding ideal timing of endoscopy.

In addition to evaluating the oesophagus and grading the injury, endoscopy also allows oropharyngeal, gastric and duodenal assessment. Gastric outlet obstruction resulted from peri-pyloric injury in as many as 5.3% of alkali-induced burns, with no associated oesophageal strictures.[59]

Endoscopy should be performed cautiously, with minimal or no air insufflation if possible, to avoid any perforation. The scope should never be advanced blindly and if an adequate view cannot be achieved or severe circumferential injury is detected, endoscopy should be terminated. Endoscopy findings should be carefully documented. Nasogastric tube placement should be considered under direct endoscopic vision. This will greatly facilitate feeding in the presence of a severe injury during the first few weeks.

We defer endoscopy if presentation is delayed beyond 48 h from injury, performing a contrast swallow and meal after 2–3 weeks to assess for strictures if the patient is symptomatic at presentation or there is a history of strong alkali ingestion.

- A *water-soluble contrast swallow and meal* is used if perforation is suspected, to identify the site and extent of perforation. Beyond the acute phase, it may diagnose secondary oesophageal strictures from 3 to 6 weeks post-injury. Gastric outlet obstruction secondary to pyloric strictures may also be evaluated. Oesophageal perforation may also be identified in the post-procedural context of oesophageal stricture dilation using contrast swallow.
- *Endoluminal ultrasound* has been used in adults to determine the extent and depth of oesophageal injury. However, experience with use of endoluminal ultrasound in caustic injuries is limited and not commonly available in low and middle income settings where most of the injuries are seen.

Table 3
Zargar grading of caustic oesophageal injury.

Grade	0	I	IIa	IIb	IIIa	IIIb
Endoscopic appearance	No evidence of injury	Mucosal erythema and oedema	Superficial non-circumferential erosion, ulcers, haemorrhage or exudate	Deep or circumferential ulceration	Multiple scattered ulcerations with patchy necrosis (brown, black or grey)	Extensive necrosis
Incidence	11–57%	11–88%	7–26%	13.6–28%	0.5–12%	0–1%
Risk of stricture formation	0%	0%	< 5%	71.4%	~100%	

Adult-size probes have hard tips and are not recommended under 15 kg of body weight,[60] and there are no reports of the use of mini-probes for this purpose. The risk of associated perforation is also unclear.

- *Computed tomography (CT)* has been used to identify perforation in adults with mediastinitis and peritonitis. CT scans offer a detailed evaluation of the oesophageal wall and perioesophageal tissues. However, the availability, accessibility and potential malignancy associated with radiation in children limits its use in caustic ingestion.
- There is no evidence to indicate that acute inflammatory markers, a full blood count or blood gas analysis contribute to diagnosing oesophageal injury.[25,48,61,62] It must however be noted that if oesophageal perforation is suspected, biochemical and radiological changes will be observed.

Definitive treatment

Most patients suffer from mild injuries and these grade 0–IIa injured patients should be observed in hospital until full oral feeds are tolerated. Patients with grade IIb and III injuries will require further evaluation and management of potential stricture development once their acute management is complete. Initial hospitalisation of 2–4 weeks is typically required in these cases before oral intake is optimal. A liquid diet, either orally or via nasogastric tube as tolerated, may initially be required in as many as a quarter of patients.[63]

Secondary prevention/modulation of strictures in the acute phase

Proton pump inhibitors (PPIs)

Reduction of stomach acid with PPIs or histamine H2-receptor antagonists is hypothesised to protect healing oesophageal mucosa and reduce stricture formation. Routine use of PPIs after caustic ingestion is widespread practice.[53] Our observation of the positive effect of gastric fundoplication in radiologically proven reflux on resistant stricture healing is supported by others[64] as well as observations of abnormal pH, manometry, and impaired oesophageal transit, in children with caustic strictures.[65] No randomised trials were found.

Oral nystatin suspension

Endogenous fungal overgrowth in the context of a disrupted oesophageal mucosal barrier may delay oesophageal healing and exacerbate stricture formation, especially if an indwelling nasogastric tube becomes colonized. We routinely prescribe nystatin until 3 weeks after ingestion or resolution of any oesophageal stricture. This practice is based on endoscopic biopsy results of chronic strictures demonstrating fungal hyphae, but little empiric evidence supports its use.

Nasogastric tube placement

In children with severe oral burns or grade IIb–III injury, nasogastric tube placement at the time of early endoscopy allows early enteral feeding, avoiding the complications of parenteral nutrition and undernutrition. An animal study of nasogastric stenting of the oesophageal lumen in rabbit-model of severe caustic ingestion showed decreased stenosis with no difference in fibrosis compared to controls,[66] suggesting that concerns about foreign body irritation on the healing oesophageal mucosa are unfounded. Potentiation of gastro-oesophageal reflux is possible, and concomitant antacid therapy is recommended.

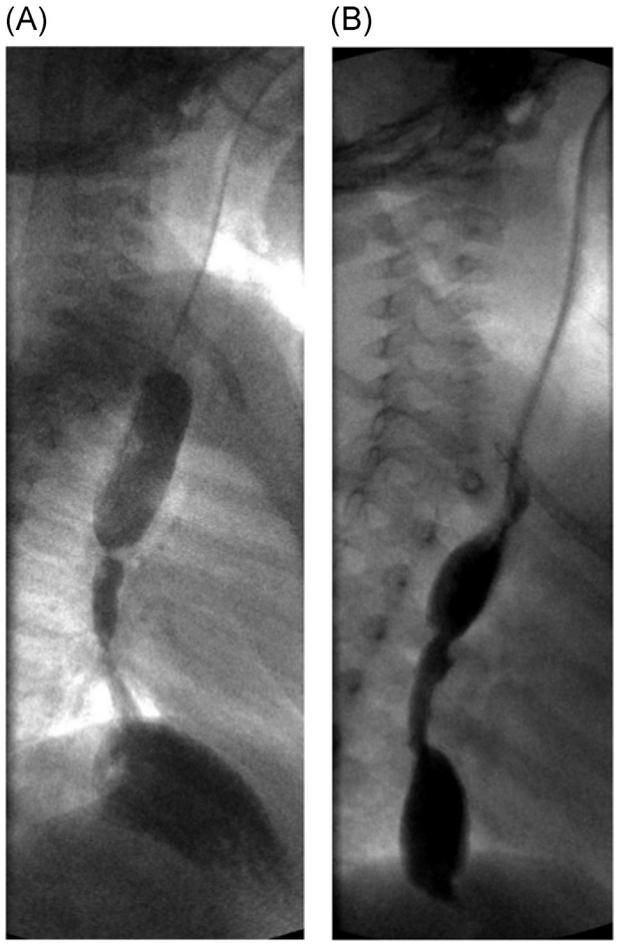

Figure. Oesophageal stricture from oven cleaner ingestion (A) 3 weeks after injury demonstrating tight mid-oesophageal stenosis with contrast hold-up on contrast oesophagogram and (B) 4 weeks after injury following stricture dilation, with interval improvement in the proximal stenosis but confirming stricture formation involving several centimetres of mid-oesophagus.

Steroids

Despite meta-analyses showing equivalent stricture rates in steroid and non-steroid-treated groups, with worse outcomes in grade III strictures where steroids were given,[67] some series report the ongoing use of steroids as standard treatment for all cases of caustic ingestion.[6,31] Animal studies support the use of systemic dexamethasone.[65] However, evidence is lacking for its clinical effectiveness, with one study of 79 patients who received intravenous methylprednisolone showing no statistical difference in outcomes compared to 167 historical controls.[68] The stricture rate of 7.1% in a large series where steroids were not used[5] were on par with or lower than rates from series where they were administered routinely. A prospective randomized trial in 30 patients receiving 2 mg/kg/day of prednisolone or oral prednisone for 3 weeks showed no significant difference in stricture rate compared to controls.[69] A recent small controlled trial of high dose methylprednisolone (1 g/1.73 m^2 daily for 3 days) in 42 patients with grade IIb caustic injury showed a significant reduction in stricture rate compared to 41 controls with no reported side effects.[70] Steroid use has been indicted in an increased perforation rate in patients with grade III burns undergoing early oesophageal dilation.[2,54,71] Large-scale randomised trials are needed to evaluate their risks and benefit.

Management of long-term sequelae

Strictures

Oesophageal strictures

Caustic ingestion is the most common cause of oesophageal stenosis in children in LMIC.[72] Early oesophagoscopy findings of a grade IIb or III injury, oesophageal stenosis on contrast oesophagogram[5] (Figure 1) and persistent dysphagia at 3 weeks after injury[51] may be used for early identification of children who require stricture dilation. Some centres report symptomatic treatment only within the first 2–3 weeks after presentation, without early endoscopy. Early dilatation (starting between 10 and 21 days) was considered only in symptomatic patients,[44] usually in conjunction with a contrast oesophagogram.[5,51] However, early endoscopic risk stratification is preferable in most settings as it avoids late detection of strictures where limited solid intake mask symptoms, and allows efficient resource-stratification for follow-up in LMIC. Stricture rates vary widely from 2%[43] to as high as 49%,[63] and predominantly affect the proximal to mid-oesophagus. *Serial stricture dilation* is the mainstay of therapy for oesophageal strictures, with oesophageal replacement reserved for extremely long and/or refractory strictures.

Dilatation programmes ideally start at 3 weeks post-injury,[5,13,51] continuing weekly as long as progress is being made in dilation calibre. Delaying stricture dilation initiation beyond 3 weeks from injury may exacerbate fibrotic stenosis and prolong the need for dilatation.[13] It is also demonstrated that delayed start of dilatation correlates with increased chance of oesophageal replacement.[13,38] Dilatation frequency is diminished once the preferred calibre for age is achieved, from every second or third week to monthly for maintenance dilatations according to symptoms.

Most children who develop a stricture will require weekly to 2-weekly dilatations for an average course of 3 months, with an average of 12 dilations.[5,38] Prolonged courses of serial dilatations have been used to preserve the native oesophagus, stretching over several years in over half in several series.[26,72] Good prognosis for successful stricture dilation includes non-lye strictures, strictures under 5 cm in length, strictures in the upper third of the oesophagus and strictures in younger patients (under 8 years of age).[72]

Prograde bouginage over a guide-wire (e.g., Guilliard-Savary dilators), placed under fluoroscopic guidance if the distal lumen is not visible endoscopically, or retrograde string-guided (Tucker) bouginage via a gastrostomy, often remain necessary for long strictures. Balloon dilators have been found to be similarly effective, and may reduce secondary scarring by gentler radial pressure rather than longitudinal shear force.[53,73,74] A perforation rate of 0.4–17.4% is reported,[5,26,74–76] higher than the incidence in congenital, reflux-associated or anastomotic strictures.[77] Karnak et al.[75] reports an 18% associated mortality with perforation at dilation and an 18% associated oesophageal replacement rate. Isolated reports of brain abscesses developing after prograde bougienage of caustic oesophageal strictures recommend prophylactic broad spectrum antibiotics to limit bacteraemia.[78]

Various adjuncts to stricture dilation attempt to reduce and modulate scar formation.

(1) *Steroids*: Steroids alter the collagen in scar tissue in animal studies, softening strictures.[79,80] Triamcinolone acetate injected serially into intractable strictures (not progressing or maintaining calibre with simple weekly dilation over 1 month) is reported to be effective.[51,81–83] Four small randomized trials in adult patients with benign strictures (with a combined total of 50 patients in the treatment groups) reported greater diameters achieved in patients in the intra-lesional steroid injection compared to controls.[84–87] Betamethasone and hydrocortisone have also been used.[82] Large multicentre randomized trials are needed to clarify indications and complication risks, as associated perforation does occur. Endoscopic guidance may improve efficacy of the injections,[88] and although a mini-probe has been used for this purpose in one report of three adults,[89] there are no paediatric reports of its use.

(2) *Mitomycin*: This fibroblast-modulator has been reported to be effective in resolving strictures with topical application via a rigid endoscope after dilation in animal studies[90] and a few small case series.[91–93] A double-blind randomised study done by Hamza et al. on 40 paediatric cases demonstrated lower dilatation requirement and higher resolution of strictures in the mitomycin group.[94] Similarly, a study comparing mitomycin injection, dexamethasone injection and saline injection in an adult cohort of 75 patients with benign oesophageal strictures showed significant improvement in the first two groups in terms of dilation frequency and symptoms.[95]

(3) Long-term *stenting* of oesophageal strictures has been reported as an alternative to serial dilations with good results.[57,64] Double-tube polyamide and silicone designs have reportedly aided stricture resolution with moderate success but have not achieved widespread use.[96–99] Stents of appropriate paediatric size may need to be custom-ordered; adult biliary and tracheal stents have been used but are not optimal. Significant trauma from stent removal of self-expanding covered metal (nitinol) stents (SEMS) may occur due to adherent granulation tissue, which may lead to secondary strictures, and requiring removal within 1–2 months.[100] Polydiaxonone absorbable stents (SX-ELLLA Stent Esophageal Degradable BD, Hradec Kralove, Czech Republic) aim to avoid this problem but are costly, and granulation hyperplasia above and below the stent may still be problematic.[101] Reported complications of stents in the small number of adult studies of stents for caustic strictures include severe odynophagia, chest pain, vomiting, stent migration, food bolus obstruction and haemorrhagic ulceration, and frequently led to stent removal or replacement.[102] Failure rates in a quarter to a third[64] due to stent migration and uncontrolled reflux add to the impetus for randomized controlled trials comparing efficacy, complications and costs of stenting with traditional dilation therapy in caustic strictures. Significant complications from pressure necrosis with fistulae and necrosis have been reported from both plastic as well as biodegradable stents[103,104] despite general satisfaction with them as an adjunct to decrease dilatations of persistent strictures under general anaesthetic.

(4) *Gastro-oesophageal reflux management* is crucial in addressing refractory strictures,[64] and should be actively investigated for in patients who are not progressing on a dilatation programme. Anti-reflux surgery should be considered if significant reflux is demonstrated on contrast meal or radio-isotope-labelled milk scan.

Oesophageal replacement

Serial dilatation of strictures may be considered to have failed if there is no sustained advancement in oesophageal calibre within 3–6 months of therapy. Risk factors for oesophageal replacement include failure to dilate the stricture at first attempt, low calibre at first dilation, average dilation sizes of 24 Fr over 1 month with poor progress, maximal dilation size at 3 months of 28 Fr, a stricture longer than 3 cm, comorbid tracheostomy for proximal

hypopharyngeal injury, and multiple strictures.[38] Oesophageal replacement was required in 5.7% of caustic strictures[5] in one series. There is no consensus on the ideal replacement conduit. Satisfactory outcomes,[105] as well as problems related to gastro-oesophageal reflux and pulmonary aspiration, has been reported with both colonic and gastric tube replacements.[106] A pedicled colonic interposition graft may be the longest achievable and best vascularised replacement conduit if oesophageal scarring extends very proximally into the hypopharynx.[107] The retrosternal route for colonic conduits is popular due to its ease of placement, with historical series reporting no adverse sequelae of leaving the native scarred oesophagus in its bed. However, in some recent series the posterior mediastinal route is preferred as both shorter and more physiological, with less colonic ectasia over time. Removal of the scarred oesophagus is also preferred where feasible due to concerns about late secondary carcinogenesis in the scarred epithelium. Anastomotic strictures at the proximal oesophageal margin are more common in caustic-associated strictures (10–45%) compared to other indications for oesophageal replacement.[107,108] Further details of oesophageal replacement will be discussed in another article in this issue.

Other stricture sites and their management

Mytomycin C injection, myectomy[109] and CO_2 laser incision[110] have been described to facilitate release of severe oropharyngeal and cricopharyngeal strictures which can impair feeding and swallowing. Strictures from severe oral and peri-oral burns can be devastating and require multidisciplinary team management.[111]

Pyloric strictures are reported in 0.8–5.4% of children with caustic ingestion.[5,59] Successful therapeutic approaches include endoscopic balloon dilation[112,113] and Finney or Heineke-Mikulicz pyloroplasty,[59] Y-V Gastric Antroplasty[114] for partial pyloric canal obstruction, or partial (Bilroth I) gastrectomy with gastrojejunostomy[5,59] for complete gastric outlet obstruction. Intra-lesional steroid injection in conjunction with balloon dilation has also been reported as successful.[115]

Oesophageal cancer

Adenocarcinoma is reported in 1–2%[116,117] of patients after caustic ingestion, representing a 1000-fold increased risk of oesophageal cancer. Overall, 1% of squamous cell carcinoma of the oesophagus has also been associated with past caustic ingestion.[118] Long-term surveillance for early detection of late secondary oesophageal carcinoma is recommended from the second into the fifth decade after injury.[118]

Other morbidity

The psychosocial impact of prolonged dilatation regimens, dysphagia-associated nutritional challenges and other long-term morbidities are poorly described in this population. A Canadian study reported a high risk of long-term antisocial behaviour as well as suicide attempts in a small longitudinal cohort of patients with caustic strictures.[119]

Mortality

Mortality in paediatric cases is much lower than in adults, as volumes ingested accidentally are normally small due to the unpleasant taste and oral burns sustained. Reported incidence ranges from 0–0.6%.[5,120] Long-term mortality attributable to secondary oesophageal cancer is unknown.

Future therapies

Animal (rat model) research

Pirfenidone, an anti-fibrotic drug and anti-inflammatory drug used to treat pulmonary and liver fibrosis as well as external scarring, has shown promise in reducing stricture formation when applied topically to the oesophagus at the time of burn.[121] Other systemic anti-fibrotics (e.g., 5-fluorouracil)[122] and anti-oxidants reduced histological evidence of damage after caustic injury.[123–125] Bingol-Kologlu reported that subcutaneously injected systemic heparin for 48 h after injury decreased collagen deposition or submucosal vascular thromboses and improved mucosal integrity in a rat study of caustic ingestion.[126] Mesenchymal stem cell transplantation therapy is being investigated,[127] with one successful case of in vivo human autologous pluripotent stem cells (on a tissue-engineered extra-cellular matrix supported by a SEMS) reported to regenerate of a perforated cervical oesophagus.[128]

Conclusion

Caustic oesophageal injuries remains a major public health issue particularly in the lower and middle income countries. Implementation of preventative measures is the only long-term solution. Management of caustic strictures is well established. New management modalities for strictures such as topical mitomycin C application are promising but require larger trials with long-term follow-up.

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