Dear editors and reviewers

Thanks for reaching out to us regarding the manuscript entitled " Utilization of Chest Tube as an Esophagus stent in Pediatric Caustic Injuries: A Retrospective Study". We believe that these comments have helped us enhance the quality of the manuscript. We also have done our best to revise as well as improve the paper according to the comments. Herewith, we provided the authors' responses to each comment right after each statement. Also, all the changes have been highlighted in the manuscript. Please feel free to contact us if you need further information.

Best regards,

Corresponding author

Reviewer #1:
Scientific Quality: Grade C (Good)
Language Quality: Grade B (Minor language polishing)
Conclusion: Major revision
Comments

This interesting study gives a good overview of paediatric corrosive injuries over a 10-year period and highlights the challenges faced in treating these injuries. It is set in a low/middle-income country and thus further raises the importance of cost-saving and innovative design in resource-limited settings.

Authors' response: Many thanks and appreciation for evaluating our manuscript.

Overall, a well-written manuscript, but the language does need to be reviewed and polished, especially in the abstract.

Authors' response: Thank you for pointing out this shortcoming. We revised the manuscript grammatically.

I would suggest including the word "Esophageal" in the title so readers know the chest tube is used in the esophagus and not in the pleural space.

Authors' response: Thank you for pointing out this matter. We added the esophageal to the title of the manuscript.

The abbreviation SEPS in the "Core Tip" should be corrected to Self-expanding Plastic Stents (from Self-Expanding Metal Stents).

Authors' response: Thank you for pointing out this matter and we do apologize for this. We have revised it.

The main focus is the description of using an inexpensive, easily available device for esophageal stenting, which might be invaluable in many settings with limited resources globally. Although an already existing device, it is being used for a novel purpose and thus in essence is a novel device. Although the device is readily available, inexpensive, and seemingly effective in this small cohort of 7 patients, there are some issues to be discussed. Firstly, using esophageal stenting to prevent or reduce future stricture formation (i.e., stent insertion in the acute phase post corrosive ingestion) is very controversial, as there is not enough evidence in either the paediatric or adult literature to support this practice as routine. The authors state in the Introduction that "Esophageal stents are considered as an effective method for preventing esophageal stricture in the first 48 hours", but this statement is not referenced or backed up by any relevant data.

Authors' response: Duly noted. Many thanks. We revised it accordingly.

Some readers might thus question why such a stent is needed and more concerningly, whether the testing of a novel device in children for a controversial indication, was formally discussed and approved by an ethics committee. I note the study was ethically approved (i.e., the retrospective reporting of the cohort and reporting of the use of the device), but was a formal discussion held regarding risk versus benefit and safety prior to using chest tubes as stents in these children? I do feel some readers might raise numerous questions about this, as the use of novel devices (especially in children) is set against rigorous safety processes in most centres globally. I think the authors need to expand on the process undertaken in making the decision on using these tubes as stents in the first place.

Authors' response: Thank you for these valuable notes. We have discussed the concerning issues:

During several years of our clinical experiences, we found that esophageal stricture has developed frequently after caustic ingestion in those who have higher grades of corrosive injuries based on the endoscopically reports. We found that esophageal stents may prevent stricture significantly; however, the recently introduced self-expanding stents were so limited and expensive in our country; and in many other low-income regions. Moreover, necrosis, ulceration, tissue hyperplasia, and fistula formation have been frequently reported by self-expandable metallic stents. After re-evaluating the patient's information, we found that esophageal stricture mostly developed in higher stages of injury (stage IIB and above). There were several recommendations from conservative management and medical therapy (such as steroids) to invasive methods; however, none of them had been proven. Therefore, we start to search for a costly and broadly available device. We consider the chest tube as an esophageal stent which

may help; however, there were several concerns about it. The expected complication could be more similar to a plastic stent rather than a metal stent. Plastic stents are said to have lesser tissue hyperplasia but with a higher rate of stent migration and a lower tendency to sustain the significant radial force. Regarding the aforementioned concern, we used the radiopaque section of the chest tube to follow its place after insertion (Fig. 3). Likewise, the external part of ECT exited the nose and fixed it to the patient's cheek using tape**.** Furthermore, we were afraid of the insertion procedure may lead to esophageal perforation, therefore, we placed it via endoscopy through a guide wire. Likewise, we didn't consider the injuries of stage IV due to its higher tendency for perforation. Moreover, we applied the anti-reflux medication and encourage the patient to elevate the head of their bed.

We added the aforementioned statements to the manuscript.

The authors make no mention as to how the 7 children who received ECT where selected compared to the other 50 in the cohort. What selection criteria do the authors suggest for using the device – how should these patients be selected? The use of stents in benign oesophageal diseases, including corrosive injuries, is a growing and evolving field and most focus lie on their temporary use for already-established fibrotic strictures. In these cases, a self-expanding stent has the advantage of being easily passed through a tight stricture and then allows for gradual opening and dilatation. The use of this ECT as a stent does not have that advantage, as the esophagus would need to be dilated to a size large enough to allow the passage of the tube. Furthermore, chest tubes are generally quite rigid and with a larger diameter, compared to undeployed SEMS, would seem to hold a higher risk of damage or perforation. As mentioned by the authors, the concern of reflux is also significant. All these factors highlight the possible risks of using this device and should be discussed.

Authors' response:

Recently, 3 types of stents are now available: Self-expanding metal stents (SEMS), plastic sent, and biodegradable (BD) stent - each with its own advantage and disadvantage. SEMS is often discouraged in benign esophageal stenosis due to its high rate of necrosis and ulceration, tissue hyperplasia, new stricture or fistula formation, and the tendency for the metal portion to embed within the esophageal wall. Plastic stents are said to have lesser tissue hyperplasia but with a higher rate of stent migration and a lower tendency to sustain the significant radial force. Both of these stents require repeated endoscopic intervention for stent retrieval. Recently, BD has been introduced in the hopes of avoiding the above complications and the need for re-intervention for stent extraction (Alvarez O, Llano R, Restrepo D. The current state of biodegradable self-expanding stents in interventional gastrointestinal and pancreatobiliary endoscopy. Rev Col Gastroenterol. 2015; 30:172–179.).

A study in 2012 compared these 3 stents in patients with refractory benign esophageal stenoses. In this study, the long-term resolution of dysphagia was highest in the metal stents group (40%)

compared to BD stents (30%) and plastic stents (10%). Tissue migration was highest in the plastic stent group and lowest in the BD stent group (10.1186/1471-230X-12-70). To date, there is still no ideal stent recommended for universal use among patients with benign esophageal strictures, the choice for each patient should be individualized (10.5946/ce.2014.47.4.295).

Therefore, currently, we have no gold stent. Furthermore, none of the aforementioned states is available in our center and many other hospitals, particularly in low-income regions.

Likewise, we used different sizes of chest tubes based on the physician's preference according to the initial endoscopic evaluation; moreover, we inserted them orally via endoscopy through a guide wire, with the narrow end positioned out of the mouth (Fig 1A). so, the risk of damage or perforation would decrease.

Several types of anti-reflux stents have been introduced in recent years; however, their efficacy is a matter of debate. Raijman et al. have found that the anti-reflux stent doesn't have any superior effect to the regular ones.

Based on our investigation the complication of reflux can be managed with proper anti-reflux medication. And no persistent reflux was reported in our cases.

The authors mention they routinely administer antibiotics and steroids in the prophylactic setting in corrosive ingestion patients. This also is controversial. Although one of the quoted studies by Howell et al showed an improved outcome, this study is now 30 years old and of low-level evidence. To date, there is collectively not enough evidence to support this as routine practice and readers might also raise this point. Two of the total 57 patients sustained injuries from boiling water – these are not corrosive injuries (corrosive or caustic injuries cause cell damage by chemical reaction and not from heat). They should thus be excluded from the analysis and would require most of the statistics to be revised.

Authors' response: Duly noted. Thank you for your great comment. As you have stated routinely administering antibiotics and steroids in the prophylactic setting in corrosive ingestion patients is controversial.

Initial studies on corticosteroid administration to prevent stricture formation in caustic ingestion were mainly on children and the results were conflicting. Methylprednisolone at a dose of 1 g/1.73 m2 per day for 3 d showed benefit in reducing stricture development (doi: 10.1542/peds.2013-3331). Likewise, dexamethasone (1 mg/kg per day) was shown to be better than prednisolone (2 mg/kg per day) in preventing stricture formation (38.9% vs 66.7%) and severe stricture development (27.8% vs 55.6%). (doi: 10.1055/s-2008-1066507)

However, another study showed that prednisolone at a dose of 2 mg/kg intravenous did not provide any benefit in preventing stricture development (doi: 10.1056/NEJM199009063231004). A systematic pooled analysis of caustic ingestion supported this finding as it failed to show additional benefits with the use of steroids in patients with grade II esophageal burns (doi: 10.1080/15563650701285420).

Based on the above evidence, it seems prudent to avoid systemic corticosteroids in caustic ingestion until further research confirms their efficacy. Therefore, we have excluded it as requested.

Regarding antibiotic administration, to date, evidence is still conflicting with regard to the use of antibiotics. A study in 1992 analyzed the utility of antibiotics together with systemic steroid administration in caustic ingestion. It was concluded that antibiotics with steroids may be useful in preventing strictures in patients with extensive burns (doi: 10.1016/0735-6757(92)90067-8). But since it was not possible to separate the effect of the antibiotic from that of the possible effect of the steroid in this study, it may be difficult to support the use of antibiotics in preventing stricture formation with such limited data. Hence, the consensus maintains that patients treated with steroids should also be treated with antibiotics (doi: 10.17352/2455-2283.000022).

Therefore, we have excluded it as requested.

What grading system was used to grade these corrosive injuries? Was this endoscopic grading, e.g., Zargar -if so, it seems strange that a patient with a grading of I landed up with a stricture requiring stenting (patient 7 of the ECT cohort)?

Authors' response: Thank you for pointing out this matter. We have used the Zarger classification. It seems there was a mistake in entering the information. Patient 7 was in grade IIB. We have revised it and also rechecked other information.

Reviewer #2:
Scientific Quality: Grade C (Good)
Language Quality: Grade B (Minor language polishing)
Conclusion: Major revision
Comments:

1. The title is misleading as the manuscript deals with a case series

Authors' response: Duly noted. Many thanks. We revised it accordingly.

2. The selection/exclusion criteria for chest tube insertion are not clear

Authors' response: Thank you for noticing this point. We clarify the criteria. The chest tube was inserted for those who had stage IIB or III of corrosive injuries.

3. How was the risk of complication due to chest tube insertion explained/justified in the methodology?

Authors' response: Thank you for this valuable note.

During several years of our clinical experiences, we found that esophageal stricture has developed frequently after caustic ingestion in those who have higher grades of corrosive injuries based on the endoscopically reports. We found that esophageal stents may prevent stricture significantly; however, the recently introduced self-expanding stents were so limited and expensive in our country; and in many other low-income regions. Moreover, necrosis, ulceration, tissue hyperplasia, and fistula formation have been frequently reported by self-expandable metallic stents. After re-evaluating the patient's information, we found that esophageal stricture mostly developed in higher stages of injury (stage IIB and above). There were several recommendations from conservative management and medical therapy (such as steroids) to invasive methods; however, none of them had been proven. Therefore, we start to search for a costly and broadly available device. We consider the chest tube as an esophageal stent which may help; however, there were several concerns about it. The expected complication could be more similar to a plastic stent rather than a metal stent. Plastic stents are said to have lesser tissue hyperplasia but with a higher rate of stent migration and a lower tendency to sustain the significant radial force. Regarding the aforementioned concern, we used the radiopaque section of the chest tube to follow its place after insertion (Fig. 3). Furthermore, we were afraid of the insertion procedure may lead to esophageal perforation, therefore, we placed it via endoscopy through a guide wire. Likewise, we didn't consider the injuries of stage IV due to its higher tendency for perforation. Moreover, we applied the anti-reflux medication and encourage the patient to elevate the head of their bed.

We added the aforementioned statements to the manuscript.

4. Why only 7 patients out of 57 underwent chest tube insertion?

Authors' response: Thank you for pointing out this matter. We only inserted a chest tube for those who had stages IIB or III of corrosive injuries. The lower grades have a less probability to develop esophageal stricture and the higher grade has a risk of perforation during stenting.

5. How was the chest tube size determined? Was the same size utilized for all 7 patients?

Authors' response: Thank you for your great comment. The chest tube's length is measured concerning age, weight, and the stature of each patient. We used different sizes of chest tubes based on the physician's preference according to the initial endoscopic evaluation.

6. Is the data for endoscopic severity grading available for comparison between 7 vs 50 cases?

Authors' response: Thank you for your wisely question. Yes. We used endoscopic evaluation for grading. 7 patients had stages IIB or III of corrosive injuries while others were classified in stages I, IIA, or IV.

7. What was the morbidity profile of the 7 patients?

Authors' response: Thank you for pointing out this matter. We have added them in Table 3.

8. Of the 7, 1 underwent colon replacement. what was the indication?

Authors' response: Thank you for noticing this point.

Colonic interposition is a surgical procedure that replaces a section of your child's damaged or otherwise underdeveloped esophagus with tissue from their colon. For one patient who had type III corrosive injury we had to replace the scarred part of the esophagus

9. How was the acceptance (pain/ discomfort/ tube dislodgement) from the patient / parental perspective?

Authors' response: Thank you for noticing this point. Sedative and analgesic medications were applied. Regarding the concern of tube dislodgement, we used the radiopaque section of the chest tube to monitor its place after insertion (Fig. 3). Likewise, the external part of ECT exited the nose and fixed it to the patient's cheek using tape.

10. Were the patients managed in the hospital during the 6-8 weeks of tube-dwelling period?

Authors' response: Many thanks for your intelligent question. Since the aforementioned 7 patients had severe injuries (endoscopy grade IIB and III), they required close monitoring.

However, we have discharged patients when they get stable and could tolerate an oral diet.

Novel therapeutic approaches for preventing or managing esophageal strictures that would enable a child to tolerate an oral diet in a more expeditious and less invasive manner would be highly desirable. Furthermore, the oblique cutting of the ECT facilitates feeding and also prevents unintentional aspiration.

11. Without a comparator arm, the chest tube utility in terms of safety, efficacy and outcome may be difficult to establish

Authors' response: Thank you for pointing out this matter. We just want to report our experience in a referral center in a low-income country. Of course, there is an inevitable need to examine during the trials. Also, we don't recommend this in the situation that another stent is available.

We added the aforementioned statements to the discussion part.

Reviewer #3:

Scientific Quality: Grade C (Good)

Language Quality: Grade B (Minor language polishing)
Conclusion: Accept (General priority)
Comments: Nothing

Authors' response: Many thanks and appreciation for evaluating our manuscript