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ORIGINAL ARTICLE

Role of Honey and Acetic Acid in Mitigating the Effects of Button Battery in Esophageal Mucosa: A Cadaveric Animal Model Experimental Study

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Abstract The objective of our study was to evaluate the role of honey and acetic acid in mitigating the mucosal injury posed by button battery using esophagus specimens from goat cadavers. This was an in vitro experimental cadaveric animal model laboratory study. We used 40 specimens of cadaveric goat esophagus and divided into four groups (A, B, C and D). The first comparison was between group A (specimens with button battery only) and group B (specimens with button battery coated with honey) for the difference in the degree of mucosal injury and change in pH and temperature. The second comparison was between group C (specimens with button battery removed after six hours) and group D (specimens with 5% acetic acid applied following the removal of the battery after six hours) for the difference in the progression of the mucosal injury and change in pH and temperature. The observer was blinded regarding the allocation of the groups. We used Fisher's exact test and independent sample *t*-test, to evaluate the statistical association. There was a statistically significant reduction in the degree of mucosal injury in specimens applied with button battery coated with honey compared to the specimens applied with button battery only. Similarly, progression of the mucosal injury was halted in specimens with the application of acetic acid following the removal of the button battery. Honey and acetic acid can mitigate the mucosal effects posed by the button battery in cadaveric goat esophageal specimens.

Keywords Button battery · Honey · Acetic acid

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Introduction

Having a habit of exploring objects with mouth and a narrow esophageal lumen, the pediatric population are more prone to get foreign bodies impacted in the esophagus [1]. Button battery in the esophagus is one of those pediatric emergencies that can often lead to dire consequences if not addressed early. The incidence of FB battery has increased over the last three decades. With an increase in the trend towards the production of larger diameter Lithium batteries, morbidities and mortalities related to battery ingestion have also increased especially in the younger children [1, 2].

The injury posed by the battery is due to the generation of OH^{-} ions resulting from hydrolysis at the negative pole of the battery. The accumulation of OH- ions thus raises tissue pH which may increase up to 10 or more. The process is usually voltage-driven and expedited with an increase in the voltage of the battery [3, 4]. It is not only the esophageal injury that is dreaded, as the alkali injury may progress to surrounding vital structures resulting in fatal complications like mediastinitis, fistulization into great vessels and bilateral abductor palsy [5–7].

Primary prevention is the key to avoid complications related to the button battery. But considering the wide availability of these batteries and their day to day use in the household electronic equipment, it doesn't always seem practical. Thus, every effort should be made to ensure the removal of the battery at the earliest along with the strategies to mitigate the mucosal effect of the alkali before and after the removal of the battery. Guidelines from national capital poison center recommend the use of honey or Sucralfate pre-operatively in cases of 12 months of age or older with the duration of ingestion within the prior 12 h because duration of ingestion above 12 h increases the risk of perforation and 0.25% acetic acid wash following removal of the battery in absence of esophageal perforation [8]. The guideline has been based on the experimental studies by Jatana et al. and Anfang et al. [9, 10]. Repeated endoscopic procedures to assess the effect of the aforementioned strategies in mitigating and halting the mucosal injury are quite inconvenient in practical situation. Thus, the rationale of our study was to further strengthen the evidence of the role of honey and acetic acid in mitigating the mucosal injury posed by button battery using esophagus specimens from goat cadavers.

Methodology

This was an in vitro experimental cadaveric animal model laboratory study conducted in the Department of Chemistry of West Point School, Kathmandu, Nepal. Approval from the research committee of the school was taken for conduction of the experiment. Goat esophagus specimens were procured from the local butcher's market. Forty small pieces, each measuring 5 × 5 cm, were made and the pieces were randomly allocated in four groups, each group having 10 specimens (Fig. 1).

Group A

Esophageal specimens with button battery to assess its effect on mucosa up to 24 h.

Group B

Esophageal specimens with button battery coated with honey to assess its effect on mucosa up to 24 h.

Group C

Esophageal specimens with button battery removed after six hours and followed up to next 18 h to assess the progress of alkali burn.

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Group D

Esophageal specimens with button battery removed and acetic acid applied after 6 h and followed up to next 18 h to assess the progress of alkali burn.

We used a brand new CR2032 3Volt Lithium battery in all specimens. In 1st comparison between group A and group B, we assessed the grade of mucosal burn and pH at 30 min, 1 h, 3 h, 12 h and 24 h. Artificial saliva containing Xylitol was used intermittently to allow a medium close to the natural environment for hydrolysis. Honey used in our study was pure and locally extracted.

The observer was blinded regarding the allocation of the groups.

The grade of mucosal injury was defined as follows:

0: No injury.

1: Involvement of superficial mucosa only.

2: Involvement of partial muscle thickness.

3: Involvement of complete muscle thickness.

4: Involvement of outer serosa.

pH was measured using litmus paper (Qualigens®, Thermo Fisher Scientific Pvt. Ltd., Mumbai, India) and compared with known standard pH color. The process was entirely subjective. pH was determined by the chemist who was also blinded regarding the allocation of the groups.

The temperature was measured with an infrared thermal gun (Microlife®, Microlife AG, Widnau, Switzerland) before the placement battery to the mucosa and after 1 h of the placement. Three readings were taken from each specimen and were then averaged. The temperature difference was then calculated. Due to poor control over the environmental temperature, only reading at 1 h was taken. During this period, the room temperature was kept static with an air conditioner to 75-degree F.

In the second comparison between group C and D, brand new CR2032 3V Lithium batteries were used. After 6 h, reading of the degree of the mucosal burn was taken. Group C was applied with artificial saliva and group D was applied with an edible vinegar (pH = 3, 5% Acetic acid), 5 ml in each specimen. The temperature was measured before and after one minute of application of acetic acid to see any immediate rise in temperature resulting from the acid–base reaction. The grade of mucosal injury and tissue pH was assessed after 24 h.

We used Fisher's exact and independent *t*-test to see the statistical association between the findings.

Results

The mucosal injury was seen within 30 min of the placement of the battery at the earliest. Specimens with button battery coated with honey (group B) had statistically significant (p-value < 0.05) reduction in depth of injury compared to specimens with button battery without honey coating (group A) at 24 h (Table 1) (Fig. 2). There was also a statistically significant difference in change in

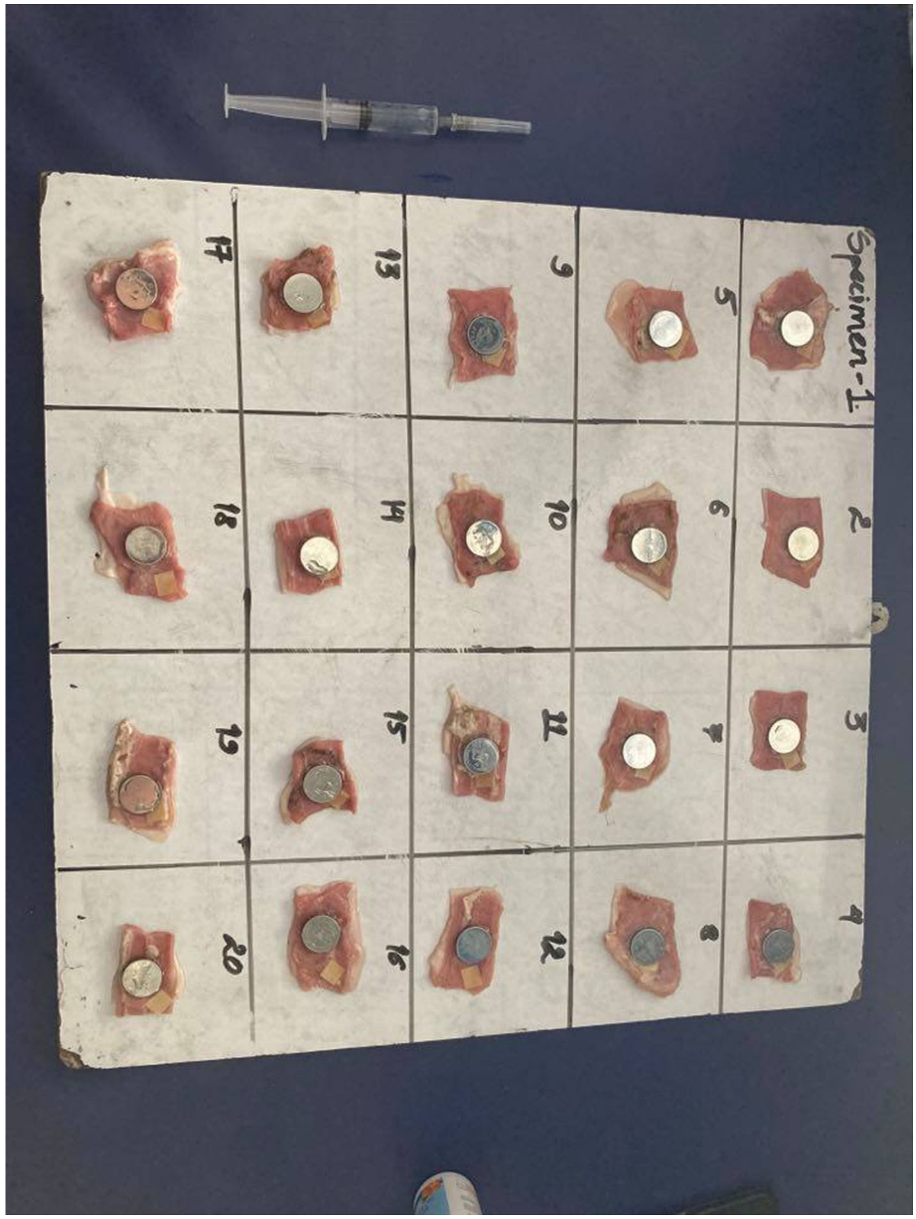

Fig. 1 Allocation of specimens with different numbers blinding the observer

tissue temperature and tissue pH between the two groups (Table 2). However, the change in tissue temperature was very nominal in both groups. Eighteen hours after removal of the button battery, in specimens where acetic acid wasn't added (group C), there was a statistically significant progression of mucosal injury. However, in specimens where acetic acid was added (group D), the mucosal injury remained static (Table 3) (Fig. 3). The difference in the mucosal injury between (group C and group D) at 18 h after removal of the button battery was statistically significant (Table 4). Following the application of the acetic acid, the average tissue temperature was raised by 0.36 °F and the average tissue pH fell from 11 to 4 (Table 5).

Discussion

A cadaveric animal model study was chosen due to the impracticability of assessing the role of honey and acetic acid in mitigating the effects of button battery at the tissue level in real case scenarios. This study showed application of honey prior to the removal of the battery and application of acetic acid after the removal of the battery were quite effective in mitigating the mucosal effects imposed by the button battery.

With an increase in the use of electronic devices which are often battery-powered, the children these days have easy access to the button batteries. A range of button batteries are available, with Alkaline, Silver oxide, Zinc-air

Table 1 Comparison of mucosal effects (grade of mucosal injury) of button battery with and without application of the honey

Group	Degree of mucosal burn					Fisher's exact test
At 30 min						
	0	I	II	III	IV	
A (Without honey)	0	10	0	0	0	*p* value:0.211
B (With Honey)	3	7	0	0	0	
At 1 h						
	0	I	II	III	IV	
A (Without honey)	0	7	3	0	0	*p*-value: 0.119
B (With Honey)	1	9	0	0	0	
At 3 h						
	0	I	II	III	IV	
A (Without honey)	0	7	3	0	0	*p*-value: 0.119
B (With Honey)	1	9	0	0	0	
At 12 h						
	0	I	II	III	IV	
A (Without honey)	0	0	4	6	0	*p*-value: 0.057
B (With Honey)	0	0	9	1	0	
At 24 h						
	0	I	II	III	IV	
A (Without honey)	0	0	0	2	8	*p*-value: 0.001
B (With Honey)	0	0	3	7	0	

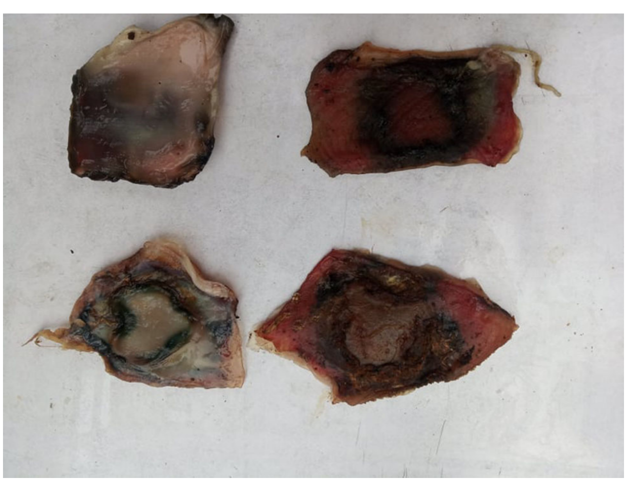

Fig. 2 Grade II injury in upper row (with application of honey) and Grade IV injury in lower row (without application of honey)

and Lithium being the common ones. Mercury batteries are no longer available in the market considering their toxicity [11]. The basic mechanism of the tissue injury by button battery is the generation of OH^- ions due to the hydrolysis of water at the junction of cathode and anode. These OH^- raise the pH of the local environment, thus causing liquefactive necrosis [9]. The tissue injury can start at 15 min, with serious injury occurring within two hours at the earliest as shown by the study of Jatana et al. [9]. The degree of injury posed by the button batteries is directly proportional to the voltage and size of the battery [3, 12]. In our study we used CR 2032 Lithium 3 V button battery as this is the most commonly available and the most commonly used one among the button batteries available in the market. "CR" in the battery denotes for Lithium/ Manganese dioxide and "2032" denotes for 20 mm diameter and 3.2 mm thickness [11]. The earliest lesion in our study was

Table 2 Comparison of change in average tissue temperature and pH induced by button battery with and without the application of honey

Group	Average tissue temperature		The average change in temperature	Independent *t*-test
	Before placement of battery	After 1 h of placement of the battery		
A (Without honey)	73.97 degree F	77.5 degree F	3.53 degree F	< 0.001
B (With Honey)	73.98 degree F	77.6 degree F	3.62 degree F	

Group	Average PH					Independent *t*-test
	30 min	1 h	3 h	12 h	24 h	
A (Without Honey)	9.5	9.5	11	11	11	< 0.001
B (With Honey)	8.5	8.5	8.5	9	9.25	

Table 3 Comparison of mucosal effects (grade of mucosal injury) at the time of removal and 18 h after the removal of button battery with and without application of acetic acid

Group C (Without acetic acid)	Grade of mucosal injury				Fisher's exact test
	I	II	III	IV	
At the time of removal	2	5	3	0	*p*-value 0.026
18 h after removal	2	0	8	0	

Group D (With acetic acid)	Grade of mucosal injury				Fisher's exact test
	I	II	III	IV	
At the time of removal	4	4	2	0	*p*-value 1.00
18 h after removal	4	4	2	0	

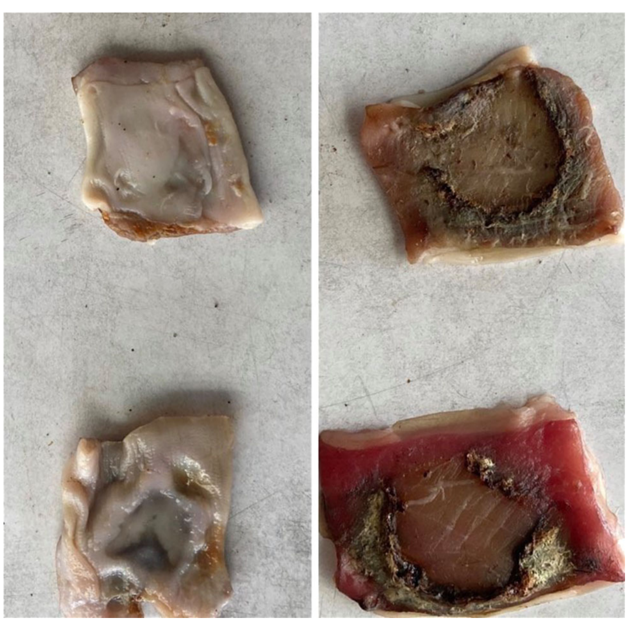

Fig. 3 Grade II injury in upper row (with application of acetic acid) and Grade III injury in lower row (without application of acetic acid)

seen within 30 min which was confined to the mucosa and the muscular layer was seen to be involved by the injury within one hour. Tissue pH rose gradually from 9.5 to 11 in specimens applied with button battery only. There was a minimal thermal reaction noted with tissue temperature rising by 3.53 °F. Jatana et al. have found similar pH changes in their study, however, they didn't observe any substantial rise in tissue temperature [9]. These observations demand the removal of the battery as soon as possible and the child once diagnosed with the button battery in the esophagus should be rushed to the operating room without any delay. Dörterler has reported the death of two months old girl, who despite the removal of the button battery within five hours, died of complications resulting from trachea-esophageal fistula [13]. Similarly, Lahmar et al. in their case series have demonstrated mucosal changes like ulceration, necrosis and bleeding in cases with button battery having a minimum mucosal contact time of two hours only [14].

Honey, in our study, showed a protective effect to prevent further progression of mucosal injury despite having a button battery in contact for up to 24 h (Fig. 2). Our

Table 4 Comparison of mucosal injury after 18 h of removal of button battery in specimens with and without application acetic acid

Group	Grade of mucosal injury				Fisher's exact test
	I	II	III	IV	
Group C (Without acetic acid)	2	0	8	0	*p*-value 0.016
Group D (With acetic acid)	4	4	2	0	

Table 5 Change in tissue temperature and PH following application of acetic acid after removal of button battery

	Before the application of acetic acid	After 1 min of application of acetic acid
Average temperature	73.63 degree F	73.99 degree F
Average pH	12	4

findings were by the study by Anfang et al. [10]. However, in contrast to their study, honey in our case didn't completely neutralize the tissue pH. There was, however, a reduction in tissue pH. Although, the duration of mucosal contact of the button battery in the study by Anfang et al. was short, both in vivo and in vitro, a significant benefit of honey was seen in reducing the extent of mucosal injury in both groups. The protective effect of honey seems to be due to its viscid consistency and slightly acidic pH. Comparing the tissues with and without application of honey (Fig. 2), a well-demarcated, deep rim of mucosal burn could be seen in specimens without application of honey and a diffuse, superficial mucosal burn could be seen in specimens with the application of honey. As per our understanding, honey prevents the diffusion of alkali deep into the tissues. The role of viscid solutions in preventing the progression of the mucosal lesion is also well shown in the study by Jia et al. In their study, edible oil applied to the esophageal specimens with button battery reduced the electrolysis and attenuated the battery discharge, thus reducing the severity of the mucosal injury [15].

Sterile acetic acid (0.25%) wash is recommended following removal of the battery if no perforation is seen in the esophagus [8]. Acetic acid, also being an edible solution, is thought to neutralize the alkali and thus halt the progression of the mucosal injury. In our study, we used commercial vinegar (5% acetic acid, pH = 3) rather than the recommended concentration of 0.25%, to assess its optimal effect. Although, there was a statistically significant reduction in the progression of the mucosal lesion, its effect on the normal mucosa wasn't assessed histopathologically, which was one of the drawbacks of our study. Even though the acid–base reaction is often exothermic, the rise in the tissue temperature was very minimal (0.33 °F) with a reduction of tissue pH from 12 to 4. Jatana et al. in their study showed the 0.25% and 3% acetic acid wash could effectively neutralize the pH and also reduce the visible eschar when compared to saline irrigation in porcine cadaveric esophageal specimens [9]. Their another study in six children who presented with button battery esophagus also showed similar results. The children after removal of the battery had 0.25% acetic acid wash over the site of the mucosal lesion. None of them developed any complications immediately as well as on follow up [16]. Sancaktar and Bakırtaş, however, had a different observation. Although 0.25% acetic acid wash in their study was able to reduce the tissue (sheep nasal septal cartilage) pH following removal of battery, it didn't show any superiority over normal saline in reducing the tissue damage [17].

In our study, histopathological examination (HPE) wasn't done in any of the specimens as the depth of injury could be easily perceived on visual inspection. However, HPE to see the effect of acetic acid on normal mucosa would have had added significant data to our study. Also, the evaluation of pH was entirely subjective. However, we minimized the bias by allowing a single person who was a chemist to assess the pH. He was also blinded regarding the allocation of the specimens.

Conclusion

Honey has a definite role in mitigating the mucosal injury posed by button battery in cadaveric goat esophageal specimens. Similarly, acetic acid (5%), following removal of the battery, also has a significant effect in halting the progression of mucosal injury. However, its lowest effective diluted solution should be used in a practical situation.

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