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A corrosive oesophageal burn model in rats: Double-lumen central venous catheter usage

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ABSTRACT

Background: We aimed to create a new and less invasive experimental corrosive oesophageal burn model using a catheter without a gastric puncture (gastrotomy). **Materials and Methods:** We conducted the study with two groups composed of 8 male rats. The experimental oesophageal burn was established by the application of 10% sodium hydroxide to the distal oesophagus under a pressure of 20 cmH_2O, via 5-F double-lumen central venous catheter without a gastrotomy. The control group was given 0.9% sodium chloride. All rats were killed 24 h after administration of NaOH or 0.9% NaCl. Histologic damage to oesophageal tissue was scored by a single pathologist blind to groups. **Results:** The rats in the control group were observed to have no pathological changes. Corrosive oesophagitis (tissue congestion, oedema, inflammation, ulcer and necrosis) was observed in rats exposed to NaOH. **Conclusion:** We believe that an experimental corrosive oesophageal burn can safely be created under same hydrostatic pressure without a gastric puncture using this model.

Key words: Corrosive burn, oesophagus, method

INTRODUCTION

Accidental ingestion of caustic agents continues to be a significant health problem in some countries.[1-4] Caustic ingestion is frequently seen in young children between the ages of 1 and 3.[3] In the United States of America, 2.3 million toxic exposures were reported in 2011, and out of the total 49% of them occurred in children 5 years or younger.[4] The oesophagus is the most common organ exposed to caustic ingestion in the upper gastrointestinal system and stricture still is a serious problem due to the corrosive ingestion.[1-6] The most widely used methods of experimental oesophageal burn were the model of Gehanno and Guedon[7] and its modification described by Liu and Richardson[8] which composed of tying both the proximal and the distal oesophagus and applying of NaOH into the oesophageal cavity.[5-10] Many antioxidants and other medications have also been tested in an attempt to prevent stricture and other late-term complications, but no therapy has become a 'standard' in clinical practice.[5,6,9,10] Discussions and research on the treatment of the oesophagus corrosive burns are still an on-going process and many agents for treatment are still being explored in experimental models. It seems that more work is needed to define the pathogenesis and the treatment of the corrosive oesophageal burn. Hence, we aimed to create an easier, simpler, reliable and standardised experimental oesophageal burn model using a single catheter without a gastric puncture.

MATERIALS AND METHODS

Animals and setting

Sixteen male Sprague-Dawley rats, weighing 220-250 g each, were selected for the study and acclimatised for 10 days in the animal laboratory of our university research centre, receiving a standard diet ad lib. The rats were then divided into two groups, equally: (1) A control group and (2) a study group. The rats were

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anaesthetised with 70 mg/kg of intramuscular (IM) ketamine hydrochloride (Ketalar, Eczacıbası, Istanbul, Turkey), and anaesthesia was maintained by additional IM injections of the same anaesthetic. After anaesthesia was obtained, a caustic oesophageal burn was created by a modified version of Gehanno and Guedon's experimental model. To create a corrosive oesophageal burn in the rat oesophagus, we used a modified double-lumen central venous catheter (double lumen cannula, Balton® Sp. z o.o, Nowy Swiat 7/14, Warszawa, Poland). As a modification, the distal-2 cm portion of the catheter was cut to prevent leakage of corrosive agent from the proximal lumen [Figure 1a-c]. Rats were kept in a supine position with the thorax elevated to 45° and a 1.5-cm midline laparotomy incision was made under the sterile conditions. A 1.5-cm abdominal oesophageal segment was isolated; the cardio-oesophageal junction was tied with 2/0 silk suture to prevent the leakage of the corrosive agent into the stomach. A 5-F, 15 cm, double-lumen catheter was placed in the upper part of the abdominal oesophagus via the mouth and proximally, just under the diaphragm, the oesophagus was tied with a 2/0 silk suture [Figure 2a and b] in order prevent aspiration of the corrosive agent into the respiratory system. The distal lumen of the catheter which corrosive substance came out through the lumen was connected to the serum set by three-way stopcock (Bıcakcılar, Istanbul, Turkey). Control group animals received 4-5 mL of 0.9% NaCl solution, while the study group animals received 4-5 mL of 10% sodium hydroxide solution, instilled through the proximal lumen of the catheter for 60 s into the isolated oesophageal segment. The solution burned the oesophagus and came back through the distal lumen of the catheter and elevated 20 cm in the serum set [Figure 2c]. Thus, the distal oesophagus was exposed to the corrosive substance at a pressure of 20 cmH_2O, and it was aimed to be equal intraluminal oesophageal pressure throughout the procedure in all animals. After 1 min of the NaOH solution exposure, the corrosive substance was evacuated via three-way stopcock and burned segment was washed for 30 s with distilled water. Distilled water was flushed continuously via the proximal lumen to irrigate the same oesophageal segment and water came out through the distal lumen via three-way stopcock. Subsequently, the catheter was then withdrawn, and the laparotomy incision was closed. All animals in both groups were killed by decapitation 24 h after exposure of the NaOH or 0.9% NaCl solution. The distal 1.5-cm oesophageal segments were harvested for histopathologic investigations

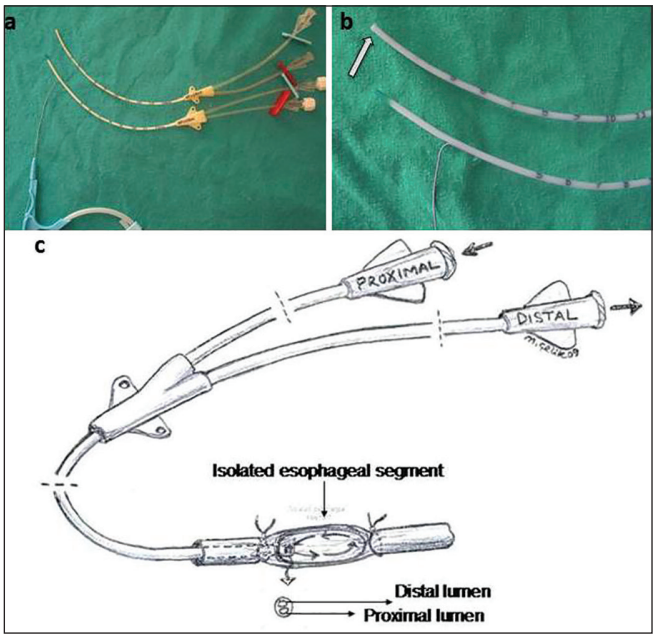

Figure 1: Photograph of a normal (a) and a modified double-lumen central venous catheter, (b) arrow shows where the catheter cut off. The corrosive substance and irrigation water came out through the distal lumen of catheter (c)

Histopathologic evaluation

The oesophageal samples were fixed in 10% neutral buffered formalin solution and embedded in paraffin. Serial sections were cut in 5 μ thick slices, stained with haematoxylin-eosin, and examined by light microscopy for the presence of tissue damage. A single pathologist examined and scored the oesophageal sections in a blinded fashion. Five microscopy fields obtained from the central part of oesophagus exposure to 10% NaOH solution or normal saline were evaluated for the presence of tissue congestion, oedema, inflammation and necrosis; each characteristic was scored as normal, 0; mild, 1; moderate, 2; and severe, 3. Ulcers were scored as present (1) or absent (0). The total tissue damage scores were calculated by adding the scores for each characteristic.

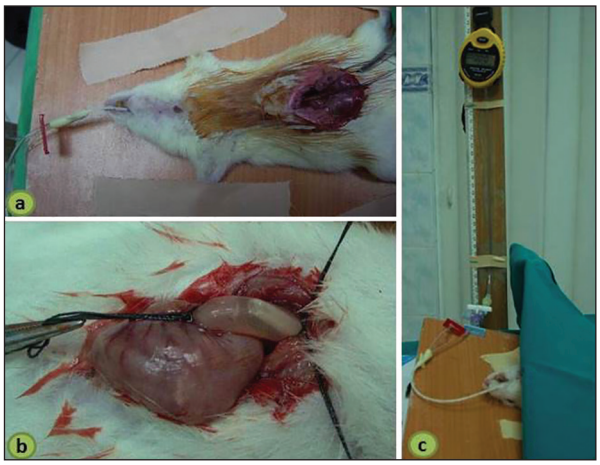

Figure 2: The steps of the experimental procedure. A double-lumen catheter was placed in the upper part of the abdominal oesophagus via the mouth (a) and the cardio-oesophageal junction was tied externally with 2/0 silk suture (b) and the oesophagus was proximally tied just under the diaphragm, and burned via proximal catheter as detailed in the text (c)

Statistical analysis

Tissue damage scores were compared with the Mann-Whitney U-test. All data were expressed as mean ± standard deviation and the statistical significance was defined as $P < 0.005$.

RESULTS

All rats survived in the experiment. The morphologic findings of the oesophagus in the control and study groups are shown in Figure 3. Oesophagi from the control group were found to be normal macroscopically. All rats had a damaged oesophagus distally and were found to be haemorrhagic oedematous and discoloured in appearance, macroscopically in the study group [Figure 1]. Oesophageal tissue damage score of the study group (4.74 ± 0.58) was significantly higher than those of control group (0.25 ± 0.46) that is, generally grade 1 and 2 in the study groups ($P < 0.005$).

DISCUSSION

Dog, cat, rabbit and rat models of corrosive oesophageal burn have previously been described in the literature. In 1981, Gehanno and Guedon[7] defined a method of rat oesophageal corrosive burn, which was an adapted model with some modifications of dog model established by Knox *et al.*[11] and Butler *et al.*'s.[12] Afterwards, Gehanno and Guedon's model was modified by Liu and Richardson. Nowadays, the two most widely used methods of the experimental oesophageal burn are the model of Gehanno and Guedon[7] and its modification done by Liu and Richardson.[8] Few corrosive burn models that believed to be less invasive have also been reported for this aim in recent years.[13-15] In the Gehanno and Guedon[7] and Liu and Richardson[8] methods, rats were placed in the dorsal recumbent position and a 2-cm midline laparotomy incision was made under sterile conditions. A 1.5-cm abdominal oesophageal segment was isolated and two catheters were placed in the abdominal oesophagus via the mouth and gastrotomy and tied with a silk suture. Animals received 2-3 mL of corrosive solution instilled through the oro-oesophageal catheter into the isolated oesophageal segment. After that, the burned segment was irrigated with water infused via the proximal catheter. However, we and the others[6,13-15] believe that gastric puncture may lead to the contamination and results mortality, especially in late phase model. Thus, we planned to perform a less invasive model of an experimental corrosive oesophageal burn in rats.

We have designed a new experimental model of corrosive oesophageal burn in adult male rats. Main differences of our method are that it does not need to perform a gastric puncture (gastrotomy), and it is possible to create corrosive burn at equal pressures to the oesophageal lumen in all rats. The most important advantage of our model is to allow the creation of corrosive burns without gastrotomy. In models with a gastric puncture, early post-operative care and feeding create complications such as contamination and septicaemia that may affect the outcome of experiments, and it may result in death.[6,9,13-15] In our method, since gastric puncture is not performed, any leakage into the peritoneum or perforation is avoided. Another important advantage of this method is that it can prevent undesirable complications such as perforation of the oesophagus because intraluminal pressure can easily be controlled. In addition, there is no risk of aspiration in case if the proximal and distal oesophageal knots are tied sufficiently. By using this method, the process can safely be completed in more sterile conditions and in a shorter period.

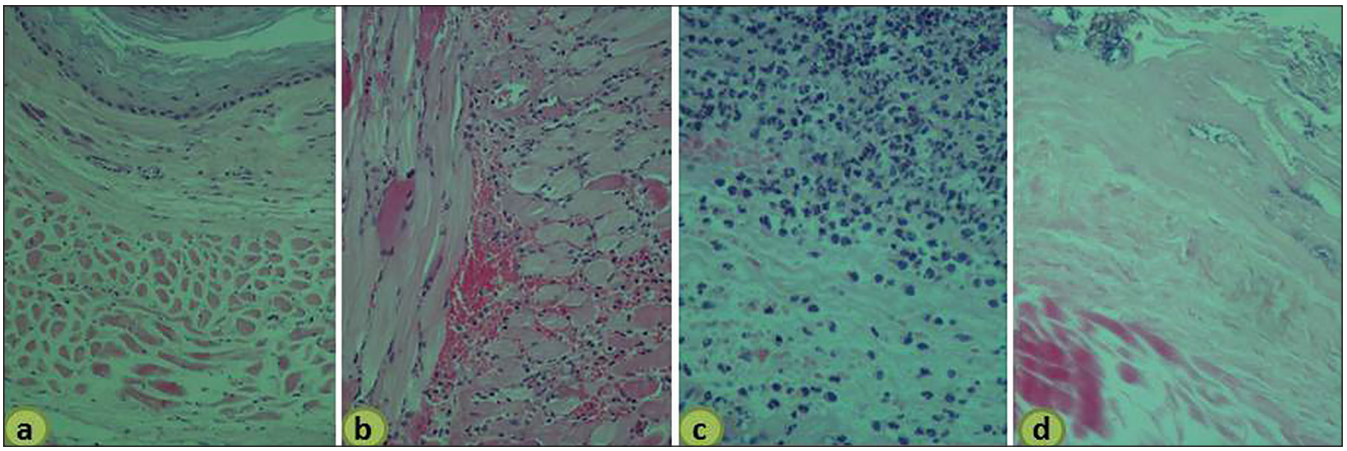

Figure 3: Normal histology of rat oesophagus in the control group; (a) (H and E, ×200) mild congestion; (b) (H and E, ×200) tissue oedema; (c) (H and E, ×400) necrosis; and (d) (H and E, ×400) in the oesophagus of a rat in study group killed 24 h after a 60-s exposure to 10% NaOH solution

One of the other advantages of our method, it is also possible to create corrosive burn under equal pressures in the oesophageal lumen in all rats of the study. This is an important advantage of our model because the same pressure can be applied in the oesophagus of all rats and this allows us to standardise the burn process. In the other models,[13-17] there is confusion in the amount of corrosive substance that should be given to create corrosive burns.[13,17] The amount of corrosive substance to create oesophageal burn in the oesophagus of rat varies from 0.3to 10 mL in the literature.[6,13-17] It has also been reported that the oesophageal volume of adult male rat is around 0.1-0.3 mL.[17] Our method allows the standardisation of the experimental model and operative techniques. Hence, there is no need to determine the amount of corrosive substances requiring for burn which varies from rat to rat accordingly its height and size. In this method, it will be sufficient to administer the corrosive agent till we reach the desired pressure. Thus, the volume of the corrosive agent is not important. Therefore, the standardisation and same safety conditions will be provided in experiments performed for each rat.

In recent years, three corrosive oesophageal burn models that believed to be less invasive have been described by Yukselen[16] Senturk *et al*.[14] and Kalkan *et al*.[15] Although, those models have been presented as less invasive and very easily applicable, they also have some drawbacks. In the methods defined by Senturk *et al*.[14] and Kalkan *et al*.,[15] the proximal edge of the abdominal oesophagus was not tied, and the rats were faced the hazardous aspiration of the corrosive agent. In our model, tracheal aspiration risk is lower as compared to other models. Another model reported by Yildiz *et al*.[17] shares aspects with ours. However, double catheter usage for the oesophageal intubation in their model is an important disadvantage. A single catheter to introduce is easy for one person, whereas handling of the two catheters is indeed hard to perform. In this regard, we can state that our method is a lot safer and easier as compared to the method established by Yildiz *et al*.[17]

CONCLUSION

We consider that this modified method is a quicker, easier and safer procedure to create the corrosive burn under equal pressure conditions in rat oesophagus and it seems a standard procedure that allows equal exposure of corrosive hazardous agent in all rats involved such experiment.

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Conflicts of interest

There are no conflicts of interest.

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