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The diagnostic utility of scintigraphy in esophageal burn: a rat model

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ABSTRACT

Background: Corrosive esophageal injury due to accidental ingestion is a serious clinical problem in children particularly in developing countries. The present study was conducted to evaluate the diagnostic utility of technetium-99m-pyrophosphate (^{99m}Tc-PYP) scintigraphy in the early stage of esophageal burns by using different concentrations of sodium hydroxide (NaOH) in an experimental rat model.

Materials and methods: Twenty-eight male Sprague–Dawley rats, weighing 200–250 g, were used in the study. Esophageal burn model was created in 21 rats by gastrically infusion of various concentrations of NaOH. The rats were divided randomly into three groups: mild-burn group ($n = 7$) received 15% NaOH, moderate-burn group ($n = 7$) received 30% NaOH and severe-burn group ($n = 7$) received 45% NaOH. Seven rats were identified as control group and received normal saline. Three hours after burn injury, 1-mCi ^{99m}Tc-PYP was administered through tail vein. Two hours after ^{99m}Tc-PYP administration, static imaging with gamma camera was performed. Then, histopathologic assessment of esophageal samples was achieved properly.

Results: All NaOH-applied groups (mild, moderate, and severe) showed a significant higher uptake ratio when compared to control group ($P < 0.005$). NaOH-applied groups displayed important histologic alterations such as mucosal disintegration, edema, inflammation, and stromal damage when compared to control group. Pearson correlation analysis revealed a significant correlation between the ^{99m}Tc-PYP uptake ratio and histologic score ($P < 0.0005$).

Conclusions: The scintigraphic imaging may provide advantages in the early stage of esophageal burns in some patients whom endoscopic procedure is contraindicated because of its high risk of complications such as bleeding and perforation.

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1. Introduction

Corrosive esophageal injuries due to ingestion of caustic substances remain to be a serious health problem in developing countries particularly in children under 6 years of age. Caustic ingestion in childhood is usually accidental, whereas ingestion by adults is frequently due to suicidal intent [1,2]. Corrosive injury typically indicates to the consumption of strongly alkaline or acidic household or industrial cleaning products. Caustic alkaline materials are found in drain openers, bleaches, and detergents containing hydrogen peroxide or sodium hydroxide (NaOH) at concentrations from 4% to 54% [1–3]. Caustic substances may lead extensive damage to the lips, oral cavity, pharynx, and the upper airway. The severity of tissue destruction depends on several factors including the type, quantity, and concentration of ingested substance, and duration of contact with the mucosa [1–5].

As indicated in numerous studies, 70% of caustic injuries are located in the esophagus. The esophageal mucosa is thought to be more resistant to acidic than alkaline substances. The type of the damage caused by acidic or alkaline substances differs significantly. Acidic agents cause to coagulation necrosis of the esophageal mucosa, whereas alkaline substances lead to liquefaction necrosis that frequently involves the destruction of epithelium, submucosa, and deep muscle layers of esophagus [1–6].

Early upper gastrointestinal endoscopy is the gold standard for assessment of the injury to the gastrointestinal tract and should be achieved within the first 24 h after ingestion [7,8]. However, endoscopy in children mostly requires to be performed under general anesthesia. In addition, as stated in previous studies, there is a certain risk of iatrogenic injury in children during endoscopy such as perforation, reversible hypoxia, and gastrointestinal bleeding [7,8]. It is evident that a minimally invasive imaging would be much better tolerated by patients than endoscopic procedure. Currently, it has been proposed that technetium-99m (^{99m}Tc)-sucralfate scanning is an accurate and specific method of screening of esophageal injury in children after ingestion of caustic substances [9]. However, ^{99m}Tc-sucralfate displays only mucosal injury by adhering to the ulcerated mucosa without presenting any evidence about the severity of lesions. Therefore, we conducted the present study to determine the diagnostic utility of technetium-99m-pyrophosphate (^{99m}Tc-PYP) scintigraphy in esophageal burns by comparing the different concentrations of sodium hydroxide in an experimental rat model.

2. Materials and methods

2.1. Animals

Twenty-eight male Sprague–Dawley rats, weighing 200–250 g each, were used in the study. The rats were kept on a 12 h-12 h light-dark cycle (light from 07.00–19.00), in quiet rooms, with 22–24°C ambient temperature. They were fed by standard laboratory food and tap water *ad libitum*. The experimental procedures used in the present study were approved by Gaziosmanpaşa University Animal Care and Ethical Committee. All experiments were carried out according to the Guide for the Care and Use of Laboratory Animals, as confirmed by the National Institutes of Health.

2.2. Study design

In our study, esophageal burn model was created in 21 rats by gastrically infusion of NaOH. All rats were anesthetized by intraperitoneal administration of 80 mg/kg ketamine hydrochloric acid (Ketalar; Eczacibasi Warner-Lambert Ilac Sanayi, Istanbul, Turkey) and 4 mg/kg xylazine hydrochloric acid (Rompun; Bayer, Istanbul, Turkey). The rats were divided randomly into three groups: mild-burn group ($n = 7$) received 15% NaOH, moderate-burn group ($n = 7$) received 30% NaOH, and severe-burn group ($n = 7$) received 45% NaOH. Seven rats were identified as control group and gastrically infused with normal saline. In this model, we reached distal esophagus of anesthetized rats by gavage and administered NaOH solution into the esophagus slowly. During this process, animals were stayed at a 90° head-up position for preventing aspiration [10].

2.3. Scintigraphic evaluation of the esophagus

Three hours after burn injury, 1-mCi ^{99m}Tc-PYP was administered through tail vein. Two hours after ^{99m}Tc-PYP administration, static imaging with gamma camera was performed in anterior and posterior positions with 2.55 zoom factor. The activity ratio between effected (E) and normal (N) esophagus area is measured by drawing rectangular regions of interest (ROI) and E/N ratio was calculated for each animal by two specialists blinded to the study groups. Then, animals were sacrificed, and histopathologic sampling was achieved properly.

2.4. Histopathologic examination of the esophagus

For histologic evaluation, formalin-fixed esophagus sections (4 μm) were stained with hematoxylin and eosin (H&E) and examined with light microscope. All sections were photographed with Olympus C-5050 digital camera (Olympus Corporation, Tokyo, Japan) mounted on Olympus BX51 microscope. In each specimen, five microscopy fields were evaluated and graded by a histologist blinded to the study groups. The burn injury was graded as normal, 0; grade 1 only the epithelial injury, grade 2 injury involving epithelium and muscularis mucosa, grade 3 injury proceeding to submucosa, grade 4 injury proceeding to inner circular muscle layer, and grade 5 full-thickness injury development [10,11].

2.5. Statistical analysis

Data analyses were performed using SPSS software (version 15.0; SPSS, Inc, Chicago, IL). Statistical differences were tested with the Kruskal–Wallis test. If the difference was significant, Mann–Whitney U test with Bonferroni correction was used. Hence, a P value of 0.0125 or below was accepted as statistically significant. Pearson correlation analysis was conducted to examine the association between scintigraphy E/N ratio and histopathologic grade of the esophagus.