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Microperforation of the colon: animal model in rats to reproduce mucosal thermal damage

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ABSTRACT

Background: The aim of the present study was to develop a rat model of colonic microperforation secondary to thermal injury for future studies to assess new treatments.
Methods: Twenty-four male Sprague–Dawley rats were used in this study. Hot biopsy forceps were used for all treatments. All lesions were created in proximal left colon using the soft coagulation setting. The power setting tested was 40 W, and the durations of monopolar soft coagulation application evaluated were 2, 3, and 4 s.
Results: In the acute phase, 48 h after thermal injury, durations of cautery of 2 and 3 s resulted in transmural necrosis, whereas with 4 s microperforation was obtained. In the late phase, 7 d after the damage, only duration of cautery of 4 s showed deep cautery effects, with signs of peritonitis.
Conclusions: We determined optimal power settings and duration of therapy in a rat model for producing electrocautery that involves transmural necrosis with microperforation.

1. Introduction

To develop medical devices, experimental models with animals are needed. The animal chosen will usually meet a determined taxonomic equivalency to humans. Experimental models with pigs are more suitable to apply the same type of devices used in clinical practice. Nevertheless, the most common animal facilities are prepared for rats or mice instead of pigs. In this sense, the rat is widely used as a laboratory animal for medical, biological, and molecular research. Rats are the smallest, lowest, and cheapest among the species suitable for colonoscopy. Having an experimental model of therapeutic endoscopy with rats would be of great interest. According to this, recently, our group described a detailed endoscopic description of the gross anatomy of the colon in rats on the basis of high-definition colonoscopy, computed tomography, and histologic assessments [1], showing that the muscular layer was thinner in the proximal left colon, 5–10 cm from the anal margin. These findings are important to decide where to perform endoscopic resections or where to induce perforations to apply endoscopic treatments because of the effects of thermal injury and coagulation necrosis of the *muscularis propria* and *serosa*. Otherwise, bowel preparation quality and comparative study with different lavage solutions before colonoscopy in rats has been analyzed [2].

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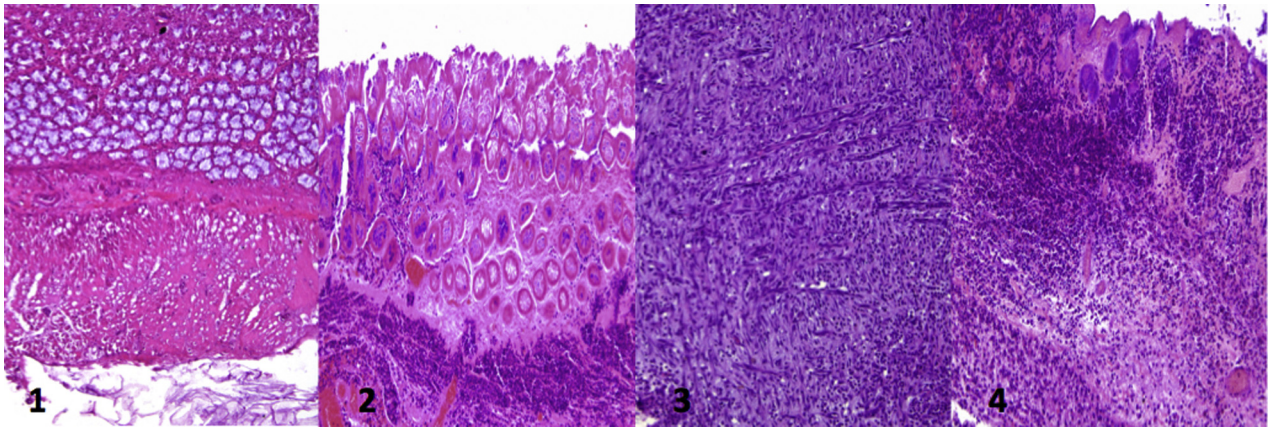

Fig. 1 – Thermal injury index. (Color version of figure is available online.)

The increased use of colonoscopy has been accompanied by a marked increase in the number of therapeutic procedures and a higher risk of transmural burn [3]. The aim of the present study was to develop a rat model of colonic microperforation secondary to thermal injury for future studies to assess new treatments.

2. Methods

Twenty-four male Sprague–Dawley rats (400–450 g) were used in this study. Rats were acclimatized for a minimum of 7 d preoperatively. Rats were kept at constant room temperature (20°C–22°C) with a relative humidity (27%–31%) with aeration under an alternating 12-h cycle of fluorescent light and darkness. The rats were housed individually in polycarbonate box cages with free access to water and food (Teklad Global 2014; Harlan Laboratories Models SL, Barcelona, Spain). Rats suffered minimal pain and distress because of the use of anesthesia. The protocol was approved by the Institutional Animal Care and Use Committee of Hospital Universitari Germans Trias i Pujol. The animals had free access to water, but food was withdrawn 8 h before the initiation of bowel preparation. A rectal enema with saline solution was performed immediately before colonoscopy.

Colonoscopy was performed with a baby upper gastrointestinal Olympus GIF-XP160 video endoscope (Olympus, Shinjuku-ku, Tokyo, Japan) with an outer diameter of 6.7 mm and a 2.3-mm working channel. Hot biopsy forceps (Olympus Medical System, Tokio, Japan) were used for all treatments. The electrosurgical generator used was the Olympus PSD-2 (Olympus Medical System). All lesions were created using the soft coagulation setting to obtain a deeper coagulation and hemostasis effect [4]. The power setting tested was 40 W, and the durations of monopolar soft coagulation application evaluated were 2, 3, and 4 s in groups of $n = 8$ rats each.

After a 24-h fasting period with free access to drinking water, rats were anesthetized by isoflurane inhalation (1.5% with 98% O_2) and placed in a supine position. Remaining faeces were flushed away by injecting water through the anus. A drop of lubricating jelly (Aquagel; Ecolab, Leeds, England) was applied on the anal sphincter to facilitate insertion of the endoscope. The endoscope was then gently passed through the anus and further introduced under endoscopic vision. Water was injected through the endoscope's working channel to visualize the lumen of the colon. Occasionally, the colon was inflated with air for better visualization of the lumen. The tip of the endoscope could be introduced to the cecum, about 24 cm proximal from the anus (see Video). The monopolar coagulation device was then passed through the accessory channel of the endoscope, and a uniform and consistent pulling force was applied to grasp the colonic mucosa in the proximal left colon, at 6 cm from anal margin, for the creation of electrocautery lesions: 40 W for 2 s (group A, $n = 8$), 40 W for

Table – Histologic level of thermal injury and diameters of lesions in proximal left colon after monopolar coagulation with a power setting of 40 W.

Duration (s)	Diameter of lesions (cm^2)		Thermal injury scale	
	48 h	7 d	48 h	7 d
2	0.39 (0.35–0.44)[*,†]	0.17 (0.15–0.18)[†]	3 (2.5–3)[†]	2 (1.5–2)[†]
3	0.54 (0.50–0.56)	0.16 (0.16–0.18)[†]	3 (3–3.5)	2 (2–2.5)[†]
4	0.56 (0.55–0.59)	0.39 (0.38–0.42)	4 (3.5–4)	4 (3.5–4)

Median (Range, percentile 25 - percentile 75).
[*] $P < 0.05$ *versus* three seg.
[†] $P < 0.05$ *versus* three seg.