THE NOVEL EXPERIMENTAL RAT MODEL OF POSTOPERATIVE PERITONEAL ADHESIONS

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The formation of postoperative adhesions is a significant clinical problem for the present-day surgery. It involves a proliferation of fibrous tissue between two anatomically different structures, causing adherence and restricted visceral mobility. Adhesion-related complications after abdominal surgery increase mortality and morbidity, can lead to chronic pain, bowel obstruction, chronic constipation, and infertility [1] and thus significantly raise the cost of medical treatment. Due to this, there is a high demand of protocols for the treatment and prevention of these postoperative complications, which in turn can be based on the information on the underlying causes and the mechanism of adhesion growth. These studies are, however, significantly complicated by the fact that the process is affected by the variety of factors such as operation conditions, which hinders the analysis of data and prevents making unambiguous conclusions. This obstacle can be overcome by designing reliable clinical models, which involves procedures to reproducibly induce adhesions in a controllable manner. Aside from the investigation, such models can be used for developing management, treatment and prophylactic measures to be applied to this condition. At the moment most existing experimental models of peritoneal adhesions include abdominal sidewall defect and/or cecal abrasion, but the results of the different works are inconsistent [2]. Thus the objective of this study was the development of reproducible and representative experimental rat model of postoperative adhesions to further assess the efficacy of various preventative strategies for this process.

For developing the model in this work we used twenty rats of the same age and mean weight (250-300 g), which were split into four groups of five rats. Prior to the operation all rats were quarantined for 3 days in the vivarium and kept in a 12:12-h light-dark cycle with food and water available ad libitum. Them the rats were anesthetized by intraperitoneal injection of 300 mg/kg of Chloral hydrate and 1 mg/kg of Xylazine, their chest hair were removed by shaving and the skin was scrubbed with ethanol. To access the abdominal cavity a 3-cm-long lower abdominal midline incision was made. In the first group (C-group), the cecum was delivered and its wall was injured by 1 minute application of a cotton pad soaked in the alkaline (1 N sodium hydroxide) solution. In the second group (CP-group), the cecum wall and its opposite parietal peritoneum both were injured by the application of the same alkaline solution. In the third group (P-group), only the parietal peritoneum was injured. After the procedure the alkaline solution was washed out completely with saline water. In all the experimental groups, after replacing the cecum intra-abdominally, the cecum wall was fixed to the abdominal wall by a non-absorbable suture to localize adhesion sites. In the control group, necrosis was not induced and the cecum was not fixated on the parietal peritoneum. The peritoneum, the abdominal muscles, and the skin were closed by two layers of continuous sutures. To prevent infections prophylactic antibiotic (50 mg/kg Tylosin) was injected intraperitoneally immediately and once daily for 4 days after the surgery. Until the rats were euthanized, they were observed every day and the postoperative wound was cleaned with ethanol, if necessary. The rats were euthanized 14 days after the surgery.

A surgeon, who was blinded with respect to the animal groups, examined the adhesion sites between the cecal and the peritoneum macroscopically. Adhesions were evaluated by a macroscopic inspection according to the rating scale from 0 to 5 proposed by Oncel et al.[3]. Grade 0 of this scale corresponds to no adhesions, while grade 1 corresponds to loose filmy adhesions that can be separated by blunt dissection. Adhesions requiring <50% of sharp dissection for separation are assigned grade 2, while adhesions requiring >50% of sharp dissection for separation as grade 3. Grade 4 and 5 corresponds to serosal injury and full-thickness injury.

After the implementation of the protocol described above, all the animals in the sham group had severe grade 0.8 adhesions. In the CP-group, all the rats had grade 5 of adhesions, but 3 animal had to be sacrificed during the postoperative course. In the P-group, two rats had grade 2 of adhesions, one rat had grade 4 adhesions, and the remaining one had grade 1 adhesions. In the C-group, severity grade of adhesions was 4.8, which demonstrated the successful establishment of the adhesions model. Obtained results demonstrate the applicability of our novel experimental model created by alkali-induced injury of the cecal wall with its subsequent fixation to using for the comparative assessment of different potential antiadhesive agents.

All experiments comply to the European Convention on Humane Treatment of Laboratory Animals [4].

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