Formation of Adhesions and Changed Activity of Tissue Plasminogen Activator of the Parietal Peritoneum of the Anterior Abdominal Wall in Rats during its Repair by Different Methods

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The effects of different methods of repair of the parietal peritoneum on the activity of plasminogen activator are studied on experimental models of adhesions. A high correlation is shown between the degree of suppression of the activity of plasminogen activator and the incidence and severity of postoperative adhesions depending on the method of repair of the peritoneum and the type of suture material.

Key Words: *adhesion process; tissue fibrinolytic activity; catgut; prolene; fibrin glue*

During the normal course of repair regeneration of the peritoneum, plasminogen turns into plasmin under the effect of plasminogen activator (PA) and dissolves the fibrinoid adhesions between abdominal organs soon after surgery [4,5,9-12]. Hence, the fibrinolytic activity of tissue plasmin depends on the activity of PA, which is present in the mesothelial tissues and in the walls of submesothelial vessels and is released during injury or under the influence of other factors [1,11,12]. A relationship between the suppression of PA activity and an increased incidence of postoperative adhesions has been demonstrated on different experimental models [4,5,11,12]. Buckman *et al.* [5] consider that the absence of prolonged local fibrinolysis is a universal pathophysiological mechanism underlying the formation of postoperative adhesions induced by various types of damage to the peritoneum.

In this study we tried to find a relationship between methods of repair of the parietal peritoneum (PP), types of suture material, and the incidence and firmness of postoperative adhesions, on the one hand, and the degree of reduction of PA activity of rat PP, on the other.

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MATERIALS AND METHODS

A total of 160 experiments were carried out on 80 adult Wistar rats weighing 180 to 200 g (4 groups, 20 animals in each). All the animals were subjected to surgery in order to induce an adhesion process in the abdominal cavity. The operations were carried out under general anesthesia by intramuscular hexenal in a dose of 100 mg/kg. The abdominal cavity was opened by a median incision, after which the lateral abdominal wall was held to the side with a special device in order to expose the PP. A 1×3-cm flap of PP was excised from both sides of the anterior abdominal wall. In the first group 10 loop sutures were made with catgut 4/0, in the second with prolene 4/0, in the third the wound was not closed (control), and in the fourth the wound surface was covered with fibrin glue after a previously described method [3]. The anterior abdominal wall was sutured layer-by-layer with continuous sutures: with catgut in group 1 and with prolene in groups 2, 3, and 4.

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TABLE 1. Incidence, Extent, Type, and Solidity of Postoperative Adhesions in Rats with the Adhesion Process Modeled by Different Methods ($M\pm m$, n=30)

Group	Incidence and type of adhesions				
	incidence (% of cases)	extent	type	solidity	total score
1	29 (96.6)	3.2±0.3	2.8±0.2	2.9±0.2	8.9±0.7
2	24 (80.0)	2.1±0.1	1.8±0.1	2.4±0.2	6.3±0.4
3	20 (66.6)	2.0±0.2	1.4±0.1	1.8±0.1	5.2±0.4
4	12 (40.0)	1.2±0.1	1.0±0.1	0.8±1.0	3.0±0.3

During the excision of PP, several biopsy specimens were taken for assessing the activity of PA of normal PP serosa.

On days 1, 3, 5, and 21 after the operation 5 animals from each group were euthanized and the abdominal organs were examined macroscopically. Biopsy specimens for measuring PA activity were taken from various areas of PP at the site of the adhesion process model. The adhesions in the abdominal cavity were counted on days 3, 5, and 21 after surgery as described elsewhere [8]. The number, dissemination, type, and density of adhesions were assessed and the results summarized using a score system. The activity of PA was assessed histochemically (by autography) after Todd's method modified by Lyutova [2].

The numerical data were statistically processed using Student's t test.

RESULTS

Results of macroscopic assessment of the status of the abdominal cavity. In group 1 in the first few days after surgery the operation wound was edematous, pasty, and cyanotic. The sites of suturing were purple-cyanotic with dot hemorrhages. Marked inflammations with pustules were seen in some places. It is noteworthy that in the majority of cases on day 1 the loops of the intestine and the omentum were loosely attached with fibrinous adhesions to the wound in some places of the anterior abdominal wall PP. During the first 3 days the loops of the intestine and the omentum were easily detached. On day 5 postoperation the number and extent of adhered intestinal loops and omentum decreased, but it was difficult to separate the adhered sites from the wound surface. On day 21 postoperation the adhesion process was represented mainly by cord-like, firm adhesions, and in 2 cases the intestinal loop and the omentum represented a single conglomerate with the wound in the anterior abdominal wall.

Similar changes, but less expressed, were seen in group 2. On day 1 the intestinal loops and the omentum loosely adhered to the PP wound surface, and these fibrinous adhesions were easily separated. On day 3 postoperation the number and density of fibrinous adhesions of the intestine and omentum with the wound surface decreased, and fibrinous adhesions were formed directly near the suture knots. On day 21 the adhesions were thinner and more solid than before.

In group 3 pronounced edema, hemorrhages, and hyperemia were seen around the wound on the anterior abdominal wall PP on the first day postoperation. Intestinal loops and omentum were loosely adhering to the wound from both sides. On day 21 there were just solitary thin adhesions along the edges of the former wounds.

In group 4 the operation wound was covered with a film of fibrin glue on day 1 after surgery. In some cases intestinal loops and omentum were loosely adhering to the anterior abdominal wall PP around these films. However, the extent and number of these fibrinous adhesions were smaller than in groups 1 and 2. These adhesions were easily separated. There were slight edemas and dot hemorrhages in the wound under the fibrin glue film. On day 5 fibrin glue remained

TABLE 2. Time Course of Postoperative Changes in the Activity of Tissue Plasminogen Activator in the Parietal Peritoneum of Rats with the Adhesion Process Modeled by Different Methods ($M\pm m$)

Group	Percent lysis in 12 h, mm^2		
	day 1	day 3	day 5
1	31.3±11.5 (20)	20.5±6.2 (23)	85.3±28.5 (20)
2	76.5±19.9 (21)	64.2±12.3 (20)	119.5±44.9 (22)
3	181.7±43.6 (20)	174.8±31.2 (21)	194.1±51.9 (19)
4	190.3±35.9 (23)	185.6±23.3 (22)	219.5±40.2 (20)

Note. Number of slices in parentheses.

as small fragments and fibers in the abdominal cavity or was absent altogether. Fibrinous adhesions formed near the suture knots.

Results of assessing the adhesion process. A manifest adhesion process was observed in 96.6% animals in group 1, in which catgut was used for modeling the adhesion process in the abdominal cavity. In group 2, where prolene was used, adhesions formed in 80% of cases. In group 3, where the PP was left unrepaired after the injury, adhesions formed in 66.6% of cases, that is, reliably less often than in the two groups in which the peritoneum was repaired with sutures ($p<0.01$). In group 4, in which the PP was repaired with fibrin glue, the incidence of adhesions was the lowest: 40%, this reliably differing from the other groups ($p<0.05$ and $p<0.001$).

The mean values of the solidity of postoperative adhesions are presented in Table 1. In group 1 the total score was 8.9±0.7, in group 2, 6.3±0.4, in group 3, 5.2±0.4, and in group 4, 3.0±0.3. The values in group 1 reliably differed from those in the other groups ($p<0.001$). In the fibrin glue group the total score reflecting the extent, type, and solidity of adhesions was lower than in the other three groups ($p<0.001$).

Results of measuring the PA activity of PP. The basal level of PA activity in a specimen of normal PP collected before surgery was 210.9±36.5 mm^2.

The results of measuring the PA activity of PP after operations using different suture materials and fibrin glue and in the control are presented in Table 2. In group 1 PA activity dropped on days 1 and 3 postoperation, while on day 5 it had a tendency to increase, but was still reliably lower than the basal level and the corresponding values in groups 3 and 4 ($p<0.05$).

In group 2 PA activity was reliably decreased at the first two investigation times ($p<0.05$), and the tendency for it to increase on day 5 was more obvious than in group 1.

A common feature in the time course of changes in PA activity during the postoperative period for the two suture groups was a marked drop on days 1 and 3 postoperation and subsequent negligible increase.

In group 3 there was a negligible reduction of PA activity on days 1 and 3 postoperation ($p<0.05$). By day 5 postoperation activity increased to reach the basal level.

In group 4 a negligible reduction of PA activity was observed only on days 1 and 3 postoperation ($p<0.05$), and on day 5 activity was higher than initially. Because of the high variability of PA values, the differences between the basal level and data in groups 3 and 4 were unreliable ($p>0.05$).

Analysis of the results showed that the use of catgut for repair of the PP wound in the anterior abdominal wall caused a manifest inflammatory process. The course of repair regeneration of the wound was often associated with the formation of coarser and more numerous adhesions than in the other groups. With prolene more solid adhesions were more frequent than in the group without suturing, which indicates that ischemia caused by suturing is the principal cause of adhesions. Moreover, the results of assessing the local fibrinolytic activity of PP tissue indicate that in groups 1 and 2 the activity of PA was reliably decreased in comparison with both the basal level and the values in the groups without suturing. The drop of PA activity was particularly marked in group 1, in which the degree of its reduction in comparison with the basal level and the other three groups was 465, 175, 231, and 461%, respectively. In group 2 an appreciable decrease of PA activity was observed, the degree of which was 144% in comparison with the basal level and 57% in comparison with group 4. The degree and duration of the decrease of PA activity depended on the type of suture and the antiadhesion barrier material used. A marked, more intensive, and more prolonged reduction of PA activity was observed in the catgut group. After the application of prolene the decrease of PA activity was sharp, but not as marked as with catgut.

Hence, the data indicate that the use of catgut for repair of a PP wound in the anterior abdominal wall caused a manifest inflammatory process. The course of repair regeneration was associated with intensive changes in the local fibrinolytic system. With prolene the inflammatory reaction of the peritoneum to surgical trauma involved an appreciable decrease of PA activity. In this group we observed coarser and more numerous adhesions than in suture-free groups, and hence we can assume that the sharp and more prolonged reduction of PA activity in PP tissue was caused by the ischemia induced by the suture tension in these two groups. However, there were fewer adhesions after prolene application than after catgut suturing and the degree and duration of PA activity reduction were less, too. This suggests that the toxic allergic effect of catgut on tissues plays a significant role in the pathogenesis of postoperative adhesions.

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Pathomorphologic Investigation of Intraorgan Arteries in Patients with Coarctation of the Aorta

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A stereotypic angiospasm develops in intraorganic arteries during coarctation of the aorta, which is characterized by different functional impacts: resistance in the basin of elevated vascular pressure and pressure and bloodflow regulation in the hypotension basin. The most marked structural changes are observed in the renal and coronary arteries. Changes in the small coronary arteries are mainly due to myocardial hypertrophy, whereas in the larger ones they are caused by the increased pressure transferred from the aorta. The degree of structural changes in the larger coronary arteries is greater than in the small arteries.

Key Words: *coarctation of the aorta; arteries; morphology*

Two circulatory basins with opposite hemodynamic regimens - hyper- and hypotension - appear in the organism during coarctation of the aorta (CA). The extracardiac (vascular) mechanisms of compensation in CA have been investigated mainly in experimental models [1,2,4,5,7-10, 12-17], except for a few works devoted to changes in the microcirculatory bed of the upper and lower extremities in patients [6].

This study was aimed at comparing the structural changes in the intraorgan arteries with opposite hemodynamic regimens in patients with CA.

MATERIALS AND METHODS

Material from 15 deceased patients with isolated preductal CA aged 5 to 52 years was used in the study. Three groups were distinguished in terms of age-specific vascular changes and physiological periods of life: the first comprising children and adolescents and the second and third adults aged under and over 35, respectively.

In order to elucidate the role of increased pressure in the aortic arch in the changes that develop in the coronary vessels, we selected a group consisting of 5 cases with congenital aortal stenosis involving fairly severe systolic overload of the left ventricle.

Specimens of tissues from the heart, brain, kidneys, spleen, and interdigital arteries of the extremities were taken for histological investigation. Paraffin embedding of the material and staining of tissues with hematoxylin-eosin and after Van Gieson (with additional resorcin-fuchsin staining of elastic tissues) were used.

Changes detected in the arterial wall were assessed using a previously proposed five-stage classification for the coronary vessels [3].

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