Modeling of Acute Experimental Peritonitis

A. A. Glukhov and I. N. Banin

Translated from *Byulleten' Eksperimental'noi Biologii i Meditsiny,* Vol. 129, No. 4, pp. 478-480, April, 2000
Original article submitted February 28, 2000

A new method of modeling of acute diffuse peritonitis was designed and tested. The method reproduces clinical picture of severe purulent process in the abdominal cavity with clear phasic dynamics and uniform (in their nature and extent of dissemination) pathological reactions, which improves reliability of experimental data.

Key Words: *peritonitis; modeling; experiment*

Pathogenetic mechanisms of acute peritonitis, and the development and testing of new methods of pharmacological and surgical treatment of this condition are the top problems of modern medicine [3,9,10,12,13].

The method used for reproduction of acute experimental peritonitis (AEP) is of exceptional importance for obtaining reliable results [2,4,11]. The methods of AEP modeling proposed by now [1,5-8] can be divided into 3 groups: 1) introduction of foreign bodies or chemicals into the abdomial cavity (AC); 2) bacterial contamination with various cultures of pathogenic microorganisms or fecal suspension through a puncture or section in the abdominal wall or perforation of the gastrointestinal tract; and 3) complex AEP models that include various combinations of methods 1 and 2. In our opinion, all these models have certain drawbacks. First, the dynamics and location of the purulent inflammatory process can vary even within the same animal group. Second, it is difficult to achieve adequate bacterial contamination; therefore, some animals die of toxicoseptic shock, while in others contamination is insufficient to induce peritonitis.

We designed a new method for modeling diffuse AEP that reproduces the inflammatory process maximally approximating clinical conditions.

MATERIALS AND METHODS

The method proposed in this paper is based on introduction of equal amounts of *S. aureus, E. coli,* and *P. aeruginosa* suspensions into the abdominal cavity of experimental animals. This microbial suspension is spread uniformly over all regions of AC by means of catheters preimplanted through perforated abdominal wall. The suspension is injected in three stages, 24 h after administration of autologous blood (7-10 ml/kg body weight) into the AC through the catheters. A suspension of $5.0\text{-}5.5\times10^{10}$ cells/kg is injected at the first stage, and then (12 h later) two injections of $2.0\text{-}2.5\times10^{10}$ cells/kg are performed with a 6-h interval.

The new method of AEP modeling was tested on albino rats of both sexes weighing 180-220 g. The rats were divided into five groups. Group 1 consisted of control rats. AEP was modeled: in group 2 by a single contamination of AC with a suspension of *E. coli* in a dose of 5×10^{10} per kg body weight; in group 3 by two injections of a of *E. coli* suspension in a dose of 2.5×10^{10} per kg body weight; in group 4 by a single contamination of AP with a polymicrobial mixture of *S. aureus, E. coli,* and *P. aeruginosa* in a dose of 5×10^{10} per kg body weight; and in group 5 by the method described in this paper.

The animals were examined 24, 48, and 120 h after AEP modeling. The tests included: evaluation of general health conditions, peripheral blood leucocyte count, concentration of medium-molecular-weight molecules (MWM), bacterial colonization of AC, complications, and lethality. After 120-h follow-up, all survivors were decapitated under ethaminal anesthesia. All rats were subjected to morphological examination.

The data were processed statistically by analysis of variance; the significance of intergroup differences was estimated by Student's *t* test.

Department of Hospital Surgery, N. N. Burdenko State Medical Academy, Voronezh

0007-4888/00/0004-403$25.00

TABLE 1. Time Course of Test Parameters in Experimental and Control Groups ($M \pm m$)

Group	Follow-up, h	Leukocytes, 10^6/liter	MWM, arb. units	Bacterial colonization, cells/ml	Mortality, %
1 (control)	—	7.00±0.36	278.60±8.78	0	0
2	24	9.11±0.38*	311.52±17.35	$(3.0\pm0.4)\times10^7$	25
	48	10.45±0.41*	354.20±28.17*	$(4.20\pm0.55)\times10^7$	41.66
	120	8.59±0.24*	320.09±19.40	$(6.10\pm0.31)\times10^3$	58.33
3	24	12.03±0.50*	361.19±20.04*	$(9.20\pm0.28)\times10^7$	33.33
	48	14.86±0.73*	395.45±16.52*	$(2.10\pm0.49)\times10^8$	50
	120	10.71±0.65*	340.50±24.73	$(3.20\pm0.12)\times10^6$	58.33
4	24	15.00±0.82*	342.58±10.28*	$(1.10\pm0.14)\times10^8$	33.33
	48	14.27±0.79*	371.14±14.73*	$(7.00\pm0.28)\times10^8$	58.33
	120	17.85±1.62*	390.25±23.8*	$(4.50\pm0.11)\times10^6$	66.64
5	24	15.05±0.16*	395.83±17.52*	$(4.50\pm0.07)\times10^9$	50
	48	21.05±0.17*	445.00±22.14*	$(1.30\pm0.68)\times10^9$	83.33
	120	—	—	—	100

Note. *$p<0.05$ in comparison to the control.

RESULTS

In group 2 rats, the first symptoms (adynamia, inappetence, and reduced unconditional reflexes) appeared 12-16 h after AEP modeling. Leukocyte count on days 1 and 2 increased significantly by 30.14% and 49.29%, respectively, in comparison with group 1, but then decreased (Table 1). The concentration of MWM and bacterial colonization of peritoneal exudate displayed the same time course. Animal mortality in this control group was maximum during the first two days of observation. Group 3 rats developed a more severe intoxication. After 24 and 48 h, peripheral blood leukocyte count surpassed the initial level by 71.86 and 112.29%, respectively, and then the severity of intoxication decreased. Pathological examination of survivors in groups 2 and 3 on day 5 of the experiment revealed hyperemia of the parietal and visceral perinoneum, inflation of intestinal loops, and the presence of turbiol exudate in the abdominal cavity. Group 4 rats displayed even more pronounced clinical signs of intoxication as soon as 6 h after AC contamination. Laboratory tests showed significant increases in leukocyte counts. The concentration of MWM progressively increased during the whole observation period. By the end of day 5, many animals were extremely severely ill, the respiration was arrhythmic and motor response to palpation of the abdomen was absent. Pathomorphological examination found purulent exudate in AP, considerable inflation and hyperemia of intestinal loops, and multiple abscesses between loops.

The most pronounced clinical and laboratory signs of intoxication were found in group 5 rats: leukocyte count increased by 200.71% by the end of the second day, and mortality rate was 83.33% within two days of AEP modeling. All rats in this group died within 5 days. Pathological examination found considerable amounts of purulent exudate, the parietal and visceral peritoneal leaflets were hyperemic and covered with fibrin deposits. The intestine was inflated due to paresis.

Thus, bacterial contamination of AC in groups 2, 3, 4, and 5 caused acute diffuse peritonitis, which was confirmed by clinical data, pathological examination, and laboratory tests. The most severe disease was found in the group where AEP was modeled by the method proposed by us.

Thus, the method of AEP modeling described in this paper allowed us to reproduce the picture of severe purulent process in the abdominal cavity with phasic changes similar to clinical course of the disease and uniform and extensive dissemination, which improves reliability of experimental data.

REFERENCES

1. V. M. Buyanov, G. V. Rodoman, G. G. Belous, *et al.*, *Khirurgiya*, No. 1, 25-28 (1997).
2. V. Ya. Glumov, N. A. Kir'yanov, and E. L. Bazhenov, *Acute Peritonitis: Organ Pathology, Pathogenesis, and Tanatogenesis* [in Russian], Izhevsk (1993).
3. V. K. Gostishchev, V. P. Sazhin, and A. L. Avdovenko, *Peritonitis* [in Russian], Moscow (1992).
4. L. A. Dezent, in: *Models, Pathogenesis, and Therapy of Hypoxic States* [in Russian], Nizhnii Novgorod (1989), pp. 23-24.
5. I. A. Eryukhin, V. Ya.Belyi, and V. K. Vagner, *Inflammation as Common Biological Reaction: Models of Acute Peritonitis* [in Russian], Leningrad (1989).
6. A. B. Kutovoii and L. V. Lozenko, *Klin, Khir.*, No. 3, 38-39 (1995).

7. N. A. Khlopov, in: *Abdominal Surgery* [in Russian], Tselinograd (1981), pp. 7-11.
8. S. A. Shalimov, A. P. Radzikhovskii, and L. V. Keisevich, in: *Manual of Experimental Surgery* [in Russian], Moscow (1989), pp. 125-127.
9. T. Koperna and F. Schulz, *Arch. Surg.*, **131**, No. 2, 180-186 (1996).
10. C. P. Artz and W. O. Barnett, *Ann. Surg.*, **155**, 756-761 (1962).
11. H. K. Sleeman, J. W. Diggs, and W. S. Hendrey, *Surgery*, **61**, 393-399 (1967).
12. M. Welch, *J. R. Soc. Med.*, **85**, No. 4, 246 (1992).
13. G. H. Wittmann, *Intraabdominal Infections: Pathophysiology and Treatment*, New York (1991).