COMBINED ACTION OF FRIBINOLYSINS OF THE PRINCIPAL AGENTS CAUSING GAS GANGRENE

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The fibrolysin titer in pathological foci produced by any one of the pathogens causing gas gangrene is lower than in infections caused by a mixture of 2 or 3 pathogens.

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The enzymes of fibrinolysin, which are found in the toxins of several microorganisms, play an important role in the pathogenesis of infectious diseases. This substance, which dissolves fibrin clots, facilitates the spread of pathogenic bacteria in the body [3, 4, 6, 8, 9]. Fibrinolysins are produced mainly by pathogens causing gas gangrene [3, 4, 10, 11], and the study of their role in the pathogenesis of gas gangrene is therefore important, especially in cases of mixed bacterial infection.

Because of published data [1, 2, 5, 6, 7, 12] indicating that bacterial fibrinolysins activate the tissue enzyme precursor, plasminogen, converting it into tissue fibrinolysin-plasmin, it was decided to study fibrinolytic activity in foci of gas gangrene infection caused by each of the principal agents – Clostidium Clostridium septicum, perfringens, and Clostridium oedematiens – separately and in various combinations.

EXPERIMENTAL METHOD

Experiments were carried out on 55 guinea pigs receiving, in the case of infection by a single pathogen, injection of a sublethal dose of a culture of Cl. perfringens strain No. 235, Cl. oedematiens strain No. 4, or Cl. septicum strain No. 59 into the thigh muscles. In infection by a mixture of two pathogens, 0.5 of the dose of the culture of each pathogen was injected, and 0.3 of a dose if the infection was caused by a mixture of three pathogens. The animals were sacrificed 24 h later. Exudate was taken from the pathological focus and affected groups of muscles. The affected tissues were placed in a specially designed press and the tissue juice was expressed mechanically, multiple dilutions made from it of between 1:5 and 1:160, and the fibrinolysis test carried out using the method of determining activity of commercial fibrinolysis preparations (Administrative Instruction of the Institutes of Vaccines and Sera, Ministry of Health of the USSR). The fibrinogen and thrombin used were obtained from the Kaunas Bacterial Preparations Factory.

Extracts were prepared concurrently from healthy muscles of the opposite limb of the guinea pigs and their fibrinolytic activity was also determined. In no case were even traces of fibrinolysin detected in the healthy tissues, whereas it was clearly demonstrated in extracts from the infected tissues of the same animals, in accordance with data in the literature [4, 10].

EXPERIMENTAL RESULTS

The fibrinolysin titers in extracts from foci of infection caused by a single pathogen were much lower than in infections caused by a mixture of cultures of Cl. perfringens and Cl. oedematiens, Cl. perfringens and Cl. septicum, or Cl. perfringens, Cl. oedematiens, and Cl. septicum. In mixed infection caused by Cl. oedematiens and Cl. septicum, the activity of fibrinolysins in the foci was only slightly higher than in infections caused by these microorganisms separately. The difference between the fibrinolysin titers in mono-infections and mixed infections was statistically significant for a combination of cultures of Cl. perfringens and Cl. oedematiens, Cl. perfringens and Cl. septicum, and of all three cultures ($P < 0.05$), but not statistically significant for mixed infection caused by cultures of Cl. oedematiens and Cl. septicum ($P > 0.05$).

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TABLE 1. Fibrinolytic Activity of Extracts from Pathological Foci Caused by Different Gas Gangrene Pathogens

Extract from pathological foci in guinea pigs infected by cultures of							
Cl. perfringens	Cl. oedematiens	Cl. septicum	Mix. of Cl. perfringens and Cl. septicum	Mix. of Cl. perfringens and Cl. oedematiens	Mix. of Cl. oedematiens and Cl. septicum	Mix. of Cl. perfringens, Cl. oedematiens, and Cl. septicum
Fibrinolysin titer						
1:5	1:5	1:5	1:40	1:40	1:10	1:20
1:5	1:5	1:5	1:40	1:40	1:10	1:40
1:5	1:5	1:10	1:40	1:40	1:10	1:40
1:5	1:5	1:10	1:40	1:40	1:20	1:40
1:5	1:5	1:10	1:80	1:80	1:20	1:40
1:5	—	1:10	1:80	—	—	1:80
1:5	—	1:10	1:160	—	—	1:80
1:10	—	1:10	1:160	—	—	—
1:10	—	1:10	—	—	—	—
1:10	—	1:10	—	—	—	—
1:10	—	1:10	—	—	—	—
1:10	—	1:20	—	—	—	—
1:10	—	1:20	—	—	—	—
1:20	—	—	—	—	—	—
n 14	5	13	8	5	5	7
$\bar{x}_{geom}$ 1:7,43	1,5	1:9,997	1:71,22	1:45,84	1:13,18	1:41,21
y_{min} 951:9,620	—	1:7,848	1:88,8	1:54,63	1:30,78	1:64,52
y_{max} 951:5,738	—	1:12,74	1:57,12	1:38,66	1:5,645	1:26,32
P —	—	—	<0,05	<0,05	>0,05	<0,05

In the next series of experiments the possibility of activation of fibrinolysins in a mixture of extracts was studied in experiments carried out in vitro. To do this, the fibrinolytic activity of tissue extracts was determined in monoinfections, and in parallel series of tubes the fibrinolytic activity of a mixture of these extracts was investigated, taken in half the dose of each extract for a study of the combined action of two extracts, and one-third of the dose of each when determining the combined action of three extracts. The results of these experiments were similar to those of the first series, i.e., the fibrinolysin titers in mixtures of extracts in vitro were higher than those of each extract separately.

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