EFFICIENCY OF PHARMACOTHERAPY IN COMBINED TREATMENT OF EXTENDED PURULENT PERITONITIS

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THE RELEVANCE OF THE PROBLEM

Despite the progression and improvement of methods of surgical interventions, the number of peritonitis spread among emergency operations performed is 20-35%, of which 19-60% of cases end in mortality. The main key factor in the etiopathogenesis of peritonitis remains the bacterial link. At the same time, the appearance of highly virulent microflora contributes to the antibiotic resistance of drugs associated with the presence of beta-lactamases [1; 2; 6; 7].

It is known that the prognosis of recovery of patients with peritonitis at 58% practically does not depend on treatment with antibacterial drugs. The key moment in the complex treatment of this disease belongs to the rehabilitation of the abdominal cavity (SBP). A widely used method of sanitation of the abdominal cavity (SBP) is currently washing with various medicinal solutions (because solutions of hydrogen peroxide 3%, furacilin solution, dimexide, sodium hypochlorite, ozonated solutions, etc.) [2; 4; 5; 9].

According to a number of scientists, the development of the method of antibacterial photodynamic therapy (AFDT) may be used to solve the above problems. It has been established that inflamed tissues tend to delay dyes – photosensitizers (FS) and therefore biological materials, such as inflamed tissue, and pathogenic bacteria, can become objects for exposure to photodynamics [3; 8].

Photodynamic therapy (PDT) requires a photosensitizer, i.e. a drug with a certain range of radiation absorption, a source of laser or LED radiation corresponding to the absorption spectrum of the photosensitizer, an endogenous factor – singlet – oxygen, it is generated during a photochemical reaction. Photosensitizers are dyes that are sensitive to light of the appropriate wavelength and are activated (excited) from it.

The purpose of the research is to develop and evaluate the effectiveness of the antimicrobial PDT method in the complex treatment of diffuse peritonitis (RP) under experimental conditions.

The material of the research was laboratory animals 161 white mongrel rats. The experimental research was performed on 161 animals of mongrel rats, with weights of 140-180 gr. All animals were in standard vivarium mode.

The work was carried out in the Central Scientific Research Laboratory (TSNIL) of the Tashkent Pharmaceutical Institute. Animals were taken out of the experiment according to the rule of humanism in relation to laboratory animals by an overdose of anesthesia. At the initial stage, we conducted experimentally in vitro studies to study the bactericidal properties of methylene blue and LED radiation in the red color range with a wavelength of 630 ± 20nm separately, then in their combination (methylene blue and LED radiation) at different concentrations and exposure time of LED radiation. At the same time, the bactericidal properties of 0.02% chlorhexidine solution were studied.

Experimental studies in vivo included 4 series. In the first series, we studied the effects of methylene blue (MS), LED radiation in the range of 640±20nm, as well as their combinations (PDT) and 0.02% chlorhexidine solution on the morphological structure of the parietal and visceral peritoneum in intact animals (n=75).

In the second series, we developed an experimental model of widespread peritonitis in 18 rats.

The third series consisted of 28 rats (control group), and abdominal sanitation (SPBP) in acute experimental peritonitis (OEP) was carried out with solutions of chlorhexidine in a dilution of 0.02%.

The last series included 40 mongrel rats and lavage was carried out by PDT using a solution of methylene blue in a concentration of 0.05%.

RESULTS AND DISCUSSION

The purpose of the first stage of research was to study the damaging effect of chemicals (methylene blue and chlorhexidine), and LED emitters on a healthy peritoneum. All studies were performed under identical conditions, simultaneously, under general anesthesia of animals. During and after the experiment, the condition of the animals was assessed by the established criteria.

The second stage of the study is the development of a model of widespread peritonitis according to Blinkov Yu.Yu. et al. [A/c: RU 2338265 from 10.11.2008]. By overdosing on anesthesia, the animals were removed from the experiment. To simulate peritonitis a fecal mixture was made, which was obtained from the colon of several rats. After the stool was mixed with saline solution, the resulting mixture was carried out through gauze napkins, and for 20 minutes the mixture was injected into the abdominal cavity of experimental animals at a dose of 0.5 ml per 100 g. The animals were in a head-down position at the same time. During puncture, the tip of the needle was occasionally changed to achieve infection of the entire abdominal cavity.

The aim of the third stage of the study was to simulate peritonitis, laparotomy, and sanitation of the abdominal cavity (SBP) with 0.02% chlorhexidine solution 24 hours after the simulation. Under inhalation ether anesthesia, mid-laparotomy was performed on experienced animals. Then the abdominal cavity was inspected, the morphological picture of the peritoneal

cavity was judged, as well as the state of the parietal and visceral leaf of the peritoneum; the amount of exudate and composition were measured, characterization was given, bacteriological seeding of exudate was obtained from the abdominal cavity, observing the rules of asepsis; a part of the parietal leaflet of the peritoneum was taken for biopsy. With the help of a syringe, the entire exudate was sucked out of the abdomen, followed by 3-4 times washing to the purity of the abdominal cavity with solutions of chlorhexidine in a dilution of 0.02%. The methods listed above did not differ from the main group of animals. The amount of chlorhexidine for abdominal lavage in the control group was 3 ml, and the exposure time was 5 minutes.

At the conclusion of the experiment, the wound of the anterior abdominal wall was sutured through all layers, animals were labeled and sent to a standard vivarium, where identical conditions were provided. All experimental animals who underwent surgery with fecal peritonitis, despite the methods of sanitation of the abdominal cavity for 3 days in the postoperative period (POP), were given antibiotic therapy with gentamicin at a dosage of 2 mg/kg per body weight, intramuscularly).

The purpose of the fourth stage of the study was to study the effect of photodynamic therapy (PDT) in the treatment of diffuse peritonitis RP and compare the results with the traditional method of abdominal sanitation SBP. During the operation, the macroscopic picture of the peritoneum in rats corresponded to the picture of acute diffuse purulent peritonitis

In the main IV series of animals, after determining the status of the abdominal cavity and the spread of the inflammatory process, the abdominal cavity was drained and a 0.05% aqueous solution of methylene blue (MS) was injected in a volume of 2-3 ml, then fluorescence diagnostics were performed to determine the degree of accumulation of photosensitizer (FS) in the peritoneum. After that, the abdominal cavity was washed with 0.9% isotonic solutions to pure waters, fibrin deposits were removed from the abdominal cavity by active aspiration with a syringe. The abdominal cavity was irradiated for 5 minutes with an LED device. As a photodynamic therapy (PDT) emitter, the VOSTOK 010203 device was used with an output power of up to 200 MW, a wavelength of 640 ± 20nm., operating in continuous mode.

For photodynamic therapy (PDT), the energy density is equal to 25 to 35 J/cm2 [4].

Experimental animals were derived from an experiment with an overdose of ether anesthesia. For comparison, we studied: hematology and blood biochemistry, intoxication indicators, histological materials, and mortality of rats with acute experimental peritonitis (OEP). In the control group, the abdominal cavity was washed with a solution of chlorhexidine in a dilution of 0.02%, which is widely used in surgical practice due to the active bactericidal action of the drug, many people know that chlorhexidine is sensitive to both gram-positive and gram-negative pathogenic bacteria.

Following the events, the antibacterial effect of photodynamic therapy (PDT) was revealed, after photodynamic therapy (PDT), regenerative functions of tissues were enhanced, early appearance of granulation in necrotic foci, acceleration of transplant time for auto dermoplasty of patients with burns [5]. The use of photodynamic therapy (PDT) for purulent wounds has great potential before traditional methods of treatment, which include treatment with antiseptics, the use of antibiotics, and antibacterial ointments. And the potential of photodynamic therapy (PDT) is: for the bactericidal action of PDT, the spectrum of sensitivity of microorganisms to antibiotics does not matter; with repeated use of photodynamic therapy (PDT), resistance to the method does not appear in microorganisms; The method has a direct bacteriostatic and bactericidal effect, with repeated use it does not affect the microorganism sideways, due to selective accumulation photosensitizer (FS) in pathogenic cells. Based on the above, we can say photodynamic therapy (PDT) is actively developing in medicine, especially in surgery.

RESUME

Despite the development of medicine, especially surgery (diagnostics, methods of surgery, postoperative measures, development of new technologies), many questions still remain unresolved and are awaiting their answers. Spilled purulent peritonitis has been and remains a formidable pathology in abdominal surgery which still requires research, development of new treatment methods, and innovative ways of cleansing from pathogenic cells of the abdominal cavity, which help to improve the results of treatment of spilled purulent peritonitis.

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