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THE USE OF WOBENZYM® TO FACILITATE INTERFERON SYNTHESIS IN THE TREATMENT OF CHRONIC UROGENITAL CHLAMYDIOSIS

SUKHIKH G.T., LOGINOVA N.S., FAIZULLIN L.Z., ZDANOV A.V., MALININA E.V., BOZEDOMOV V.A.

Scientific Center of Obstetrics, Gynecology and Perinatology of the Russian Academy of Medical Sciences and the International Institute of Biological Medicine, 117815, 4 Oparin Street, Moscow, Russia.

Summary: *Chlamydial infections are recognized as a major cause of infertility in couples and different types of pathology of male and female reproductive functions. Female endocervical smears and male urethral swabs were examined by polymerase chain reaction (PCR) in 3,200 patients. Optimal schedule of treatment of chronic urogenital chlamydiosis using proteolytic enzymes (peroral tablet of Wobenzym®, Mucos Pharma, Geretsried, Germany) were proposed by us. In order to realize the mechanism of the therapeutic effect of proteinases we investigated the changes in the interferon system of patients. We found significant decrease of IFN α-γ production and increase of serum IFN. Application of Wobenzym® led to normalization of leukocyte capability to synthesize IFN in response to all inductors. Standard antibiotic therapy led to chlamydia elimination in 61% women and 45% men; combination of antibiotic therapy with Wobenzym® resulted in 92% cases with women and 89.5% with men, respectively. The blockade of interferon synthesis by leukocytes seems to be the cause of long-term prolongation of chlamydial infection inducing inflammation in the genital tract. Proteinases coming into the blood relieve the blockade of non-specific antibacterial defense. Thus, proteolytic enzymes were shown as a highly efficient strengthening factor for antibiotic therapy of urogenital chlamydiosis.*

Introduction

Chlamydial infection is thought to be a major cause of infertility and inflammatory processes in the female and male urogenital system (1). Nevertheless, optimal approaches for effective treatment of chlamydiosis have not been fully developed. The schedules of antibiotic therapy commonly applied are not effective enough because they often change the infection to a hidden form and increase the probability of selection of resistant strains (2). The i. m. injection of trypsin, chymotrypsin and other proteinases was shown to significantly enhance the efficacy of chlamydiosis treatment and the application of proteinases may be a prospective treatment for chlamydiosis (3). However, the injection of proteinases frequently causes pain and may induce allergic reactions. Thus, we investigated therapeutic capabilities of Wobenzym® administrated *per os.* This pharmaceutical product is produced by MUCOS Pharma in tablets containing a combination of plant and animal proteinases.

Materials and methods

Patients. The study involved 121 females and 106 males who came to our clinics because of inflammato-

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ry diseases of the urogenital organs and/or infertility associated with chlamydiosis. Three groups of patients were formed by randomization. The first group, consisting of 41 females and 29 males, received vibramycin and tarivid for 10 days. The second group, consisting of 40 females and 39 males, received the same antibiotics in two-fold decreased dosage and had intramuscular injections of chymotrypsin for 20 days. The third group, consisting of 40 females and 38 males, received decreased dosage of antibiotics and Wobenzym® *per os* (15 tablets per day for 20 days). Once treatment was finished a follow-up using control examinations was conducted after 2 and 12-14 weeks.

Examination for chlamydiosis. Male urethral swabs and female endocervical smears were tested by PCR to examine the infection with *Chlamydia trachomatis* as previously described (4). All the patients were tested for specific antichlamydial antibodies and were found to be seropositive.

Interferon system evaluation. Patients' interferon system was studied by measurement of interferon serum levels, leukocyte spontaneous production of interferon and leukocyte interferon reaction (LIR), which was induced by agents indicated in Table I. The interferon levels were measured in bioassay. The interferon activity unit was implied as 50% inhibition of cytopathic action of encephalomyocarditis virus (EMC) on monolayer of human embryo fibroblasts M-19 (5). The levels of serum interferon were measured by titration of serum from venous blood.

Table I *Characterization of the inducers of interferon synthesis used in the study*

Interferon inducers	Type of induced interferon
Newcastle disease virus (NDV)	interferon α
Ridostin, larifan	interferon α/β
T-cell mitogens (PHA, Con A, SEA)	interferon γ

Results and Discussion

The data on efficacy of enzyme therapy and common antibiotic therapy of chlamydiosis are presented in Table II. In the first group of patients treated with antibiotics only 61.4% of the patients recovered completely. The treatment with antibiotics, combined with intramuscular injection of chymotrypsin or administration of Wobenzym® *per os,* resulted in >90% treatment success. All patients recovered had no recurring chlamydial infection for the 3 months following the treatment.

In order to determine the mechanism of therapeutic effect of proteinases we studied changes of interferon system in dynamics. Leukocyte response to all inductors used was significantly decreased in males and females infected with chlamydiosis. The response to IFN-α inducer (Newcastle disease virus, NDV) was five to six times lower than the normal range and was found to be the most suppressed. The response to IFN-γ inducers (ConA, PHA and SEA) was 1.5-2-fold below the normal range and the response to IFN-α and IFN-β inducers (larifan and ridostin) was 1.3-1.5 below the normal range. At least four of six parameters of LIR decreased in all females and males studied (Fig.1).

Treatment with antibiotics alone did not enhance LIR for all inducers studied. Moreover, improvement of LIR was not observed in patients who were successfully treated for chlamydiosis with antibiotics.

Table II *Proteases increase the efficacy of antibiotic treatment of chlamydiosis*

Treatment schedule	Number of patients	Recovered from chlamydiosis	
		Absolute numbers	%
Antibiotics	70	43	61.4
Antibiotics + Chymotrypsin	81	73	90.1
Antibiotics + Wobenzym	78	72	92.3

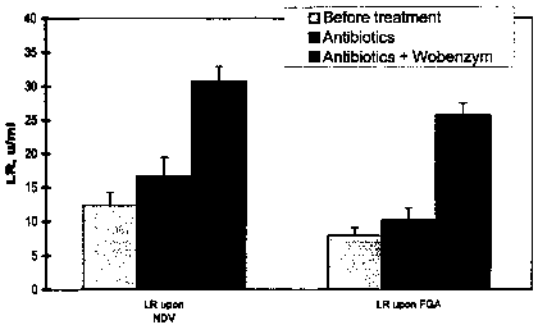

Fig. 1 The change in leukocyte response (LR) to α/β-IFN inducers for different methods of therapy of urogenital chlamydiosis.

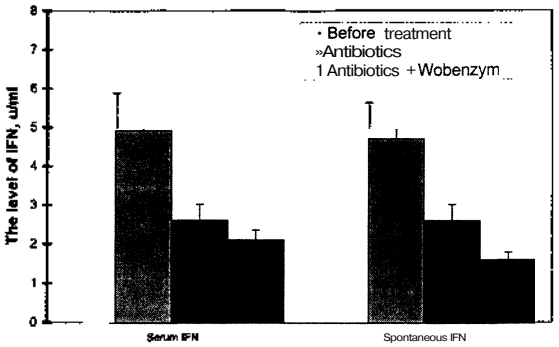

Fig. 2 The change of the levels of serum and spontaneously produced IFN in different methods of therapy for urogenital chlamydiosis.

The use of Wobenzym® significantly increased and recovered the ability of leukocytes to produce IFN in response to all inducers.

The response of lymphocytes to IFN-α inducers recovered after 24 h in 58% of the patients treated with Wobenzym®, while the same response recovered after 72 h in patients treated with chymotrypsin. The response to IFN-γrecovered after 48 h in 73% of patients treated with Wobenzym®, while the same response recovered after 72 h in 59% of patients who received intramuscular injections of chymotrypsin. The treatment with enzymes recovered t levels of serum interferons and the leukocyte spontaneous production of interferon (Fig. 2).

The blockade of interferon production by leukocytes seems to be a cause of prolonged chlamydial infection that develops under slow inflammatory process in the genital tract. Once they are in the blood, proteinases disrupt the blockade and recover the system of effective nonspecific antibacterial defense.

Wobenzym® seems to have almost the same therapeutic efficacy as α-chymotrypsin. However, none of the patients receiving Wobenzym® *per os* experienced an allergic reaction or other side effects. Almost all the patients receiving chymotrypsin complained about the pain from the injection. Of the 81 patients injected with chymotrypsin, there were several cases of side effects. Nine patients were found to have sleepiness interfering their life style; one patient had nasal bleeding twice, seven patients had allergic reaction such as urticaria, one patient had Quincke's edema. The mentioned side effects arose after 7-8 injections of chymotrypsin. The use of Wobenzym® did not induce side effects other than giddiness that arose during the first days of the treatment and disappeared after 2-3 days.

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