Izatizon, As an Izatin-Thiosemicarbazone Derivative, Has Antiviral, Anti-Tumor Actions and No Side Effects

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Abstract: Our long lasting researches of izatizon - izatin-thiosemicarbazone derivative, were confirmed by studies of many scientists who worked in this field. Izatizon, like many thiosemicarbazone derivatives exhibits antiviral, antibacterial, anticancer properties and also possesses immunomodulatory effect, which enables its wide applications in the clinic and veterinary medicine.

Key words: *izatin-thiosemicarbazones, izatizon, antiviral, immunomodulatory, anticancer properties, urology diseases.*

I. INTRODUCTION

Since the middle of the previous sentury beta-tiosemicarbazons of izatin with different substitutes are considered as very perspective. They have found their application in the chemoprophylaxis and viral disease treatment. β -tiosemicarbazons N-methyl- and N-ethylizatin are the most active among them. Their antiviral effect is resulted from the action on RNA- polyribosome and DNA- polyribosome nuclease complex, expressed by viral reproduction inhibition and immunomodulating activity. [1, 2, 3, 4].

Izatin β -tiosemicarbazon decreases reproduction activity of smallpox vaccine virus, it also inhibits rhinovirus and flu virus reproduction. It is determined that Izatin β -tiosemicarbazon activates alkalotic DNKase and inhibits acid DNKase. It completely decreases reproduction of smallpox virus, flu A, parainfluenza of the 3-d type, arboviruses and adenoviruses. [5].

Antiviral action of tiosemicarbazon class compounds concerning RNA-containing viruses was determined. [6] Tiosemicarbazon and marboran derivatives delay viral reproduction of different groups of viruses: poliomyelitis, rhinoviruses, mixoviruses and paramyxoviruses. Molecular mechanisms of these compounds has been studied, and found out that they were very effective and have a wide influence spectrum due to increased penetration into the organs and tissues. This leads to the inhibition of viral intracellular reproduction and bacterial infection [7].

During the study of the mechanism of action of the metysazon it was noted that along with the positive actions observed some negative effects of the drug. In this regard, Potopalsky et al in 1980 has solved this problem by inventing a unique solvent for the metysazone (marboran) as a result of that izatizon was created. . Izatizon is a composite preparation composed of substances that are used as independent tools in medical practice, namely the metysazon, DMSO and PEG-400 [8, 9].

Izatizon is a new generation drug that combines the antiviral activity and immunomodulatory effects, and in addition has anticancer properties, especially in relation to melanoblastoma. It has been experimentally proved that izatiaon affects both viruses and cellular mechanisms of the immune system. In model systems of herpes virus and adenovirus we detected that izatizon has the ability to stimulate the activity of reparative DNA synthesis. [10].

Immunomodulatory properties of izatizon has been discovered and interpreted. [9]. It was also found out that a wide range of izatizon biological activities is based on the structure of the molecule of metysazon - the main active component of the drug, and depends on the properties of the solvent and micro environment [11]. Izatizon has the ability to inhibit the thymidine kinase activity of the herpes virus and the adenovirus, which leads to the inhibition of the virus in the early stages of infection. We discovered the curative effect of izatizon under the herpes virus infection and adenoviral infection, and its availability at AIDS, tuberculosis and viral hepatitis C. Our data shows the convincing significance of this drug, especially nowadays, when all the continents of the Earth face the dramatic increase of the number of viral and immune aggressive diseases, that were considered to have disappeared, as well as emergence of new ones, among which the virus diseases occupy an important place. Izatizon is active against DNA-and RNA-containing viruses. It also has pronounced immunomodulatory properties [9].

Izatizon is an activator of nonspecific resistance factors through its stimulating effect on the expression of metabolic and phagocytic function of macrophages, and its influence on natural killer cells activity and synthesis of lysozyme [12].

Izatizon is one of the most perspective preparations that is able to increase specific and nonspecific resistance indexes during immune status violations and possesses antiseptic and antiphlogistic characteristics. Preparation action is based on good penetration through demytilsulfoxide (izatizon component) mucous membranes and transferring of other components (metysazon, twin) to the organism tissues. Izatizon components possess antiviral, antiphlogistic, antihistaminic, analgesic, antimicrobial and fibrinolytic characteristics. Moreover, the preparation is able to restore antimicrobial antibiotic activity against resistant or weakly sensible to it bacteria strains [13].

According to the research results we assumed that this preparation has to be on point position in the prophylaxis and treatment of many urological diseases. Izatizon showed itself as a preparation of the wide activity spectrum with the significant curing effect [13,14]. This effect was achieved due to combination of antiseptic, anti-inflammatory, antifungal, antivirus beharacteristics. Izatizon gives a significant economical effect: decreasing the treatment time, it is handy in use (water solutions, spreads easily cope with other medications), does not lead to the complications, allergies, reduces the number of visits to the doctor. No contraindications are shown.

Izatizon was used in complex treatment of male uresis system under viral and inflammatory diseases [15].

Medical collective of the urological department of the Road hospital N_2 of the Stryy station use izatizon for prostate and urethra inflammatory diseases treatment and also they use it like antiviral and antitumoral preparation during the last 5 years.

Chronic prostatitis is one of the most diffuse diseases of the male urinary and sexual systems. Information about its treatment has been well known since ancient times but still we cannot answer exactly on all the questions of the disease pathogenesis and its treatment. The search of new means for prostate inflammatory disease therapy is one of the main tasks of modern urology.

The research program includes gathering of complaints, anamnesis, physical examination, clinical analysis, prostate secreta examination, instrumental examination: ultrasonic diagnostics and cystoscopy. The preparation was used as a microclyster 30-50% of water solution or together with 10 ml. 2% of lidocain, once or twice a day during ten days.

The preparation was used for the treatment of 40 patients with acute attack of chronic prostatitis in complex with regular therapy. Except this, another (control) group (30 men) was observed. They were treated during the acute attack of chronic prostatitis only with habitual antiphlogistic therapy. Then the results of both groups were compared.

Improvement of health, symptomatology decrease, clinical analysis improvement were observed on the 4-6 day of the therapy in the patients group which was treated with izatizon, while in the control group the same result was observed on the average 7-10 day of the treatment. Relying on this it became possible to reduce antibacterial preparation application together with izatizon to 7-10 days. Antibiotic therapy average course in the control group was 14 days.

While the patients examination during the whole year, repeated prostatitis exacerbations were observed three times (3 persons) in the first group, that was 7,5%, and five times (5 persons) in the second group, that was 16,7%. Izatizon microclysters were used to treat the disease relapses in the first patients group, their condition became stabilized and in the control group, we had to use antibiotic therapy.

Among preparation side effects, the most common is burning feeling in the application area. The addition of 2%-6-10 ml. of lidocaine solution was successfully used against this defect. It removed or reduced significantly side effects and did not influence the treatment course.

So, izatizon is a medical system where all ingredients are active. Each of them controls its personal inflammation factor: excessive aquation, necrosis, infection inhibition, pain syndrome, evacuation and infection inhibition on the initial phase, regeneration process stimulation on the second phase of the inflammation process.

Except izatizon application for prostatitis treatment, it was also widely used against pointed condyloma. We have treatment experience of 10 patients and the obtained results were good. Izatizon was applied as applique on condyloma three times a day as a result candylomas of six patients have disappeared and have significantly decreased on the rest of the patients.

Based on previously mentioned we can claim about positive effect of izatizon application during prostate inflammatory disease treatment and pointed condylomas. It also decreases antibacterial preparation usage, prolongs relapse-free clinical course and it can be introduce for public application. This preparation has excellent prospects in human medicine.

REFERENCE:

- Bauer D.J.Clinical experience with the antiviral drug marboran (N-methiylisatin-3-thiosemicarbasone) // Ann. N.-.Y. Acad. Sci. -1965. – N130. - P. 110-117.
- [2]. Bauer D.J., Apostolov K., Selvay J.W.T. Activity of metisazone against RNA viruses //Ann.N.-Y.Acad. Sci.-1970.- Vol.173. № 1. - P. 314-319.
- [3]. Patskovsky U.V., Negrebetskaya E.N., Chernomas A.A., Voloschuk T.P., Kitam O.E, Rubashevsky E.I., Tereschenko M.J., Nosach I.N., Potopalsky A.I. Aromatic thiosemicarbasones: their antiviral action and interferon/ The decreasing of adenovirus type-1 resistance against interferon by methisazone in vitro // Biopolymers & Cell -1996.- Vol.12.- N 2. P. 74-83.
- [4]. Conolly J.N. Thiosemicarbazone derivatives in pox-virus infections // Practicioner.-1966.-Vol.197.- P. 373-380.
- [5]. D.J. Bauer, L. St. Vincent, et al., Prophylaxis of Smallpox with Methisazone, American Journal of Epidemiology, Volume 90, (Issue 2), August 1969, pp. 130-145.
- [6]. Sheffild F.W., Bauer D.J., Stephenson S.M. The protection of tissue cultures by isatin-B-thiosemicarbazone from the cytopathic effacts of certain pox viruses // Brit. J. Exper. Pathol. - 1960.-XL1, N 6.-P. 638-647.
- [7]. Gungate G. V., M. A. Richter Isatin and its derivatives. Chisinau.- Stiinta. 1977. -P. 220.
- [8]. A.I. Potopalsky, L.V. Lozyuk, Izatizon is an Antiviral and Antitumor Drug (Naukova Dumka, 1995. -P.175).
- [9]. L.A. Zaika, O.I. Bolsunova, A.I. Potopalsky, Antiviral, Antitumor and Immunomodulatory Properties of Izatizon Drug (Kolobih, 2010).
- [10]. Zayika L.A, Bolsunova O.I, Patskovskiy U.V., Rubashevskiy E.L., Dyadyun S.T., Rybalko S.L., Potopalsky A.I.// Antiviral drug izatizon has no mutagenic effect and stimulates the proliferation of cells of the immune system. – Biopolim.Cell. - 1995.-V.11, N 5.- 69-78 p.
- [11]. Ol'ha I. Bolsunova, Ol'ha O. Brovarets', Dmytro M. Hovorun, Leonid A. Zaika, Anatoliy I. Potopalsky// Quantum Chemical Analysis of Structural and conformational Properties of Methisazone and Prototropic Tautomerism of Isatin. IREBIC.- 2011. -V. 2. № 5. -159-`165.
- [12]. Zaika LA, Bolsunova AI, AI Potopalsky, VA Malyzhev. Izatizon affects the cytotoxic activity of natural killer (NK) // Imunol and Alerhol. -2002.- No1. - S.43-45.
- [13]. Bauer D.J. Clinical experience with the antiviral drug marboran (N-methiylisatin-3-thiosemicarbasone) // Ann. N.-.Y. Acad. Sci. -1965. – N130. - P. 110-117.
- [14]. Anatoly Potopalsky, Olga Bolsunova, Leonid Zaika. MOLECULAR GENETIC RECOVERY OF THE ENVIRONMENT AND HUMANS – THE WAY TO INCREASE THE PROFITABILITY OF AGRICULTURE AND THE WELFARE OF PEOPLE // No 9 (2016): <u>GISAP</u>: Biology, Veterinary Medicine and Agricultural Sciences –P. 9-12
- [15]. Zhyrun Y.V., Miroshkin V.O., Zhyrun V.N., Feldman M.Y., Ostapovich Y.M., Experience of Izatizon application for male uresis system treatment under viral and inflammatory diseases "BASES OF MOLECULAR-GENETIC HEALTH IMPROVEMENT OF BOTH HUMAN AND ENVIRONMENT" 31 May - 1 June 2005 Kyiv.Kolobig. p. 65-67.