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MALABSORPTION SYNDROME AS A MANIFESTATION OF SYSTEMIC EFFECTS IN ADVANCED FORMS OF PULMONARY TUBERCULOSIS

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Abstract. As of October 2012 84 countries had reported at least 1 case of extensively drug resistant tuberculosis (EDR TB). In November 2012, the WHO epidemiological surveillance stated: all new TB cases in the world are 3,7 % of multi-drug resistant tuberculosis (MDR TB); 60,0 % of MDR TB among the new cases of TB are documented in Brazil, China, India, and South Africa.

Key words: tuberculosis, multi-drug resistant tuberculosis, fluoroquinolones, malabsorption syndrome.

Introduction. Pathology of the gastrointestinal tract (GI) ranks the third place on comorbidity in patients with lung tuberculosis (LTB). As early as in the late XIX century the notion of "pretuberculosis dyspepsia" emerged [4, 7]. It was due to the fact that in some of patients with an unclear diagnosis, who complained of steady loss of appetite, weight loss, discomfort in the epigastric region, and had been visiting a doctor for years, pulmonary tuberculosis was revealed later on [1, 8].

A significant incidence of comorbidity is explained not only by related pathogenetic factors of diseases, but by adverse effects of drugs on the gastrointestinal tract in patients with LTB, the spread among the latter, burdened with social and behavioral factors [2, 5]. One of the reasons for inefficient treatment in LTB is malabsorption of anti-TB drugs taken per os, which causes insufficient drug concentrations in blood and lesions, which favour development of chemoresistant TB [1, 8]. Excessively expressed syndrome of the systemic inflammatory response in TBL contributes to the development of a malabsorption syndrome [1, 6, 8]. So, to resolve the problem of effective treatment a parenteral route of administration of anti-TB medicines should be recommended for patients with TB and gastrointestinal comorbidity.

Aim: to evaluate the clinical efficacy of oral and intravenous anti-TB treatment in the intensive phase of chemotherapy (IFHT**)** in patients with pulmonary MDR TB.

73 patients were included in the open-label randomized study (74,3 % male, 25,7 % female) aged 20 to 76 years. **Criteria** – patients with newly diagnosed pulmonary MDR TB.

Materials and Methods: clinical, laboratory, X-ray, microscopy, microbiology, statistics.

We compared the efficacy of oral and injectable fluoroquinolones in patients with MDR TB. Levofloxacin (Lfx) – tablet form was used in 43,9 % of patients, injectable form – in 40,4 % (Leflocin by "Yuria-Pharm", Ukraine); moxifloxacin (Mfx) – (Maxicin by "Yuria-Pharm", Ukraine) in 8,8 % of patients; gatifloxacin (Gfx) – (Bigaflon by "Yuria-Pharm", Ukraine) in 7,0 % of patients.

All patients included in the study by selection of pairs in form prevalence of tuberculosis process and the severity were divided into four groups.

I – 25 patients. In IFHT Lfx was used in a dose of 1000 mg orally for 8 months; II – 23 patients. In IFHT Lfx was used intravenously – 1000 mg per day for a month. And then 1000 mg – orally for 7 months; III – 11 patients. In IFHT Mfx was applied intravenously (infusion concentrate of 20 mg/ml) 400 mg per day for a month (does not require dose adjustment in patients with impaired liver and kidney function), followed oral intake of 400 mg for 7 months; IV – 14 patients. In IFHT Gfx 400 mg (infusion solution 0,4 % 200 mL) was applied intravenously per day for a month. Then orally 400 mg for blisters for 7 months.

Results and discussion. While analyzing the effectiveness of chemotherapy in tablet and injection forms Lfx (in a month) sputum microscopy results showed, that sputum conversion in group I took place in 20 % and in patients of group II – in 37,3 % ($p<0,05$). Normalization of complete blood count in group I was recorded in 24,0 % of patients, in group II – in 34,8 % respectively ($p<0,05$). The absence of

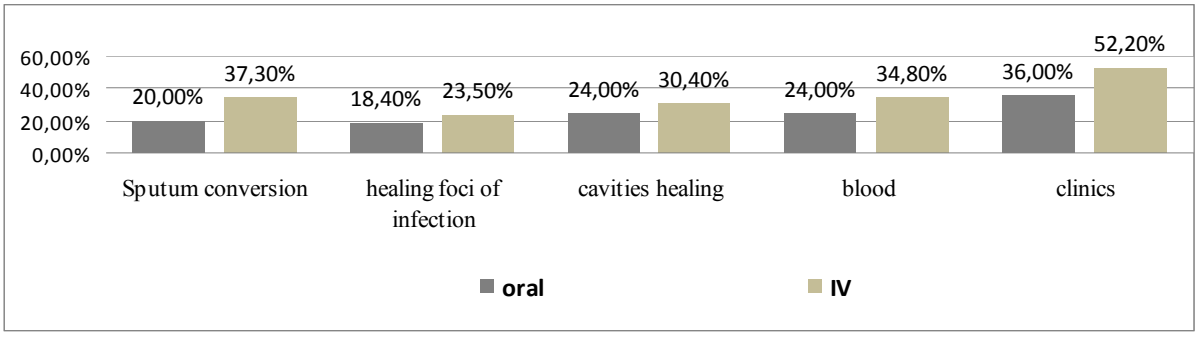

Fig. 1. Analysis of the effectiveness of chemotherapy in tablet and injectable forms Lfx (in 1 month)

Table 1

Profile MDR TB	II group (N=23)	III group (N=11)	IV group (N=14)
HR	E + Z + Km + Lfx + Et	E + Z + Km + Gfx + Et	E + Z + Km + Mfx + Et
HRS	E + Z + Km + Lfx + Et	E + Z + Km + Gfx + Et	E + Z + Km + Mfx + Et
HRSE	Z + Km + Lfx + Et + Cs + PAS	Z + Km + Gfx + Et + Cs + PAS	Z + Km + Mfx + Et + Cs + PAS
HRZEt	Z + Km + Lfx + E + Cs + PAS	Z + Km + Gfx + E + Cs + PAS	Z + Km + Mfx + E + Cs + PAS
HRSEZ	Z + Km + Lfx + Et + Cs + PAS	Z + Km + Gfx + Et + Cs + PAS	Z + Km + Mfx + Et + Cs + PAS
HRSZ	E+ Z +Km + Lfx + Et + Cs	E+ Z +Km + Gfx + Et + Cs	E+ Z +Km + Mfx + Et + Cs

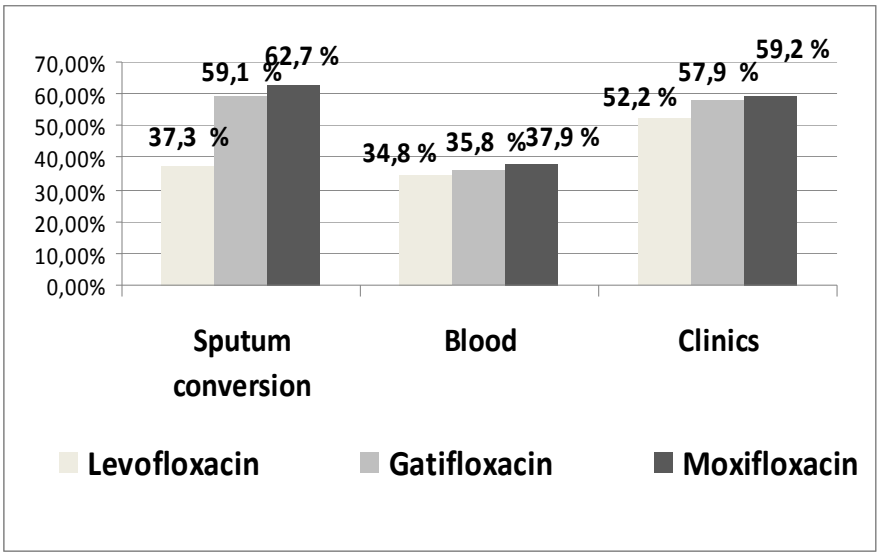

Fig. 2. Comparative characteristic of injectable fluoroquinolones 3rd and 4th generations

major clinical manifestations of tuberculosis in group 1 was observed in 36,0 % of cases and in group II – in 52,2 %, respectively ($p<0,05$).

Thus, studies have confirmed the higher efficiency of the use in an intensive phase (one month) of chemotherapy programs for MDR TB patients injectable Lfx versus tablet form. Intergroup value of indicators is different significantly, p=0,01.

Individual modes of antimycotic therapy for patients of groups II, III and IV were formed according to drug sensitivity test (BACTEC method) [3].

Assessment of individual chemotherapy regimens for clinical and laboratory parameters was performed a month after the use of injectable fluoroquinolones of the 3rd and 4th generations (Lfx, Gfx and Mfx).

Analysis of the data in dynamics showed, that at prescription of Mfx in regimes of chemotherapy (after a month) cessation of bacterial excretion was observed in 62,7 % of patients, Gfx – in 59,1 %, Lfl – in 37,3 % respectively. Normalization of complete blood analysis in groups II, III and IV after a month of treatment was in 34,8 %, 35,8 % and 37,9 % respectively. Absence of main clinical manifestations after a month of treatment at prescription of Lfx was observed in 52,2 % of cases, Gfx – in 57,9 %, Mfx – in 59,2 % respectively.

The effectiveness of different programs with using fluoroquinolones of the 3rd and 4th generations (1 month) at the end of the intensive chemotherapy phase: efficacy in gr. II was 90 %: in gr. 3 – 98,2 %; in gr. 4 – 97,1 % due to the high percentage of complete resorption of focal infiltrative changes and cavities healing, which are epidemiologically important indicators for monitoring the spread of tuberculosis infection.

In the comparative analysis of the efficiency of injectable fluoroquinolones of the 3rd and 4th generations in patients with MRTB the fourth generation demonstrated significantly higher efficacy.

Thus, benefits of injectable administration of anti-TB drugs: 100 % bioavailability, quick achieving high concentrations of the drug in the lesion focus, regardless of the state of the digestive tract, the characteristics of the diet and comorbidities, reducing the number of side effects, possibility to intensify treatment, reduction of cases of therapy interruption (100% control), accurate dosing.

Conclusions

1. Malabsorption syndrome is a common comorbid condition in most tuberculosis patients. Thus, studies have confirmed the higher efficiency of the use in an intensive phase (one month) of chemotherapy programs for MDR TB patients injectable Lfx versus tablet form. Intergroup value of indicators is different significantly, p=0,01. Intravenous introduc-

tion of anti-TB chemotherapy is recommended in all tuberculosis patients with poor absorption.

2. The comparative analysis of the efficiency of treatment at prescription of injecting fluoroquinolones of the 3rd and 4th generations in group 2 is 90 %, in the group 3 – 98,2 % in group 4 – 97,1 %, due to the high percentage of complete resorption of focal infiltrative changes and scarring decay cavities that are epidemiologically important indicators for monitoring the spread of tuberculosis infection.

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СИНДРОМ МАЛЬАБСОРБЦИИ КАК ПРОЯВЛЕНИЕ СИСТЕМНОГО ЭФФЕКТА ПРИ РАСПРОСТРАНЕННЫХ ФОРМАХ ТУБЕРКУЛЕЗА ЛЕГКИХ

Л.Д. Тодорико, И.В. Еременчук, В.П. Шаповалов, Т.И. Ильчишен

Резюме. По состоянию на октябрь 2012 года 84 страны мира сообщили хотя бы об одном случае туберкулеза с расширенной резистентностью (РРТБ). В ноябре 2012 года эпиднадзор ВОЗ констатировал: среди всех новых случаев туберкулеза в мире 3,7 % это мультирезистентный туберкулез (МРТБ); 60,0 % случаев МРТБ в мире установлено в Бразилии, Китае, Индии и Южной Африке.

Ключевые слова: туберкулез, мультирезистентный туберкулез, фторхинолоны, синдром мальабсорбции.

СИНДРОМ МАЛЬАБСОРБЦІЇ ЯК ПРОЯВ СИСТЕМНОГО ЕФЕКТУ ПРИ ПОШИРЕНИХ ФОРМАХ ТУБЕРКУЛЬОЗУ ЛЕГЕНЬ

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Резюме. Станом на жовтень 2012 року 84 країни світу повідомили хоча б про один випадок туберкульозу із розширеною резистентністю (РРТБ). У листопаді 2012 року епіднагляд ВООЗ констатував: серед усіх нових випадків туберкульозу у світі 3,7 % це мультирезистентний туберкульоз (МРТБ); 60,0 % випадків МРТБ у світі установлено в Бразилії, Китаї, Індії, та Південній Африці.

Ключові слова: туберкульоз, мультирезистентний туберкульоз, фторхінолони, синдром мальабсорбції.

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